The New England
Journal of Medicine

Copyright, 1942, by the Massachusetts Medical Society

VOLUME 226 JANUARY 1, 1942 NUMBER 1

BLAST AND CONCUSSION IN THE PRESENT WAR*

JOHN F. FULTON, M.D.†

NEW HAVEN, CONNECTICUT

THE first definition of a bomb in the *Oxford Dictionary* is "a ball of wilde-fire." The Spaniards, it seems, quite early developed technics for burning enemy ships by projecting fire balls at their adversaries' sails and wooden decks; so that the first bombs were, strictly speaking, incendiaries. Later, mortars were developed for hurling explosive incendiaries. These explosive balls of fire became in the course of time less fiery and more highly explosive, and in the nineteenth century they came to be known as "bombshells." By the end of that century and during the last war, bombshells became just "shells," and the word "bomb" was reserved for explosives dropped from the air — or from the pocket of a discontented agitator.

The Nazis were the first to develop air bombing technics on a large scale: not only bombs of the high-explosive variety — screeching, bouncing and parachute bombs — but also "balls of wilde-fire" in the form of incendiaries, many of them diabolically arranged so that, when a firefighter attempts to smother them, they explode, showering hot burning magnesium in the faces of their victims. When attacking ships and objectives in England during the last two years, the Germans have used five types of high-explosive shells, the 50-kilo, 250-kilo and 500-kilo aerial bombs and the 500-kilo and 1000-kilo land mines.

PHYSICAL CHARACTERISTICS OF BOMB DESTRUCTION

The 50-kilo bomb, which has been used in such profusion over the London area, produces destruction within a sharply circumscribed space for a width of 20 to 25 feet in brick dwelling houses, such as one encounters on Commonwealth Avenue or Marlborough Street, Boston; and if one of these houses were struck, one might expect, if British example were followed, to see signs of "Business as Usual" on both sides of the 25 feet of gutted building. Similarly, when such a bomb strikes the middle of the street, it penetrates beneath the surface before exploding and then lifts up a heap of dirt over an area 20 to 30 feet in diameter and 3 to 5 feet in depth, depending on the character of the surface. The resulting crater presents a hazard to traffic. Taxicab drivers navigating in the blackout become accustomed to dropping into craters of this sort but are so skilful that they generally stop their cars when the back wheels are on the edge, quietly back out, and take another street. In England, bombing even of the 50-kilo variety is serious: since the winters are mild, the essential services are buried to a depth of only 2 or 3 feet. Almost invariably, therefore, a bombing episode in the street results in interruption of all five services — water, gas, electricity, sewerage and telephone; however, the demolition squads work with incredible speed, and generally within ten or fifteen hours all the services are repaired and the streets repaved. But all this requires a close-knit organization on the part of a dozen agencies and utilities, and I should think that the sooner such an organization is worked out on the eastern seaboard of the United States, the less the inconveniences of bombing would be felt when the time comes for the enemy to strike. We have the rich experience of the English people at our disposal. We have seen their mistakes. We have seen their magnificent reorganization on the basis of those mistakes, and I can only hope that we may profit by them.

The 250-kilo bomb creates greater havoc, but again the area of destruction is sharply circumscribed, being limited to 100 to 130 feet of four-story brick construction; if the bomb strikes in the middle of the street, the crater is 75 to 100 feet in width and 8 to 10 feet in depth. Windows may be broken at considerable distances — up to 200 or 250 yards — from the blast wave.

*Read, in part, before the Maryland Psychiatric Society, Baltimore, Maryland, on Wednesday, October 8, 1941, and in modified form under the title "Bombs" before the New England Postgraduate Assembly, Cambridge, Massachusetts, October 29, 1941.

From the Laboratory of Physiology, Yale University School of Medicine.

†Sterling Professor of Physiology, Yale University School of Medicine.

The 500-kilo or 1000-pound bomb, of which, fortunately, the Germans have been able to use very few, is incredibly destructive and may, if it happens to strike favorably, demolish the greater part of a city block. The effects of the blast wave in the air and through ground-shock may topple buildings at a distance of several hundred yards, and the results of a given detonation of this size of bomb are as bizarre and unpredictable as they are destructive. Much the same thing may be said for the land mine, which, coming down by parachute, may destroy the greater part of a city block. No details concerning the so-called "superbomb" that the British are now using are available, but it is evidently "super" in the sense of having greater weight; if it is true that the British are using bombs weighing 1 to 2 tons, the havoc wrought in closely built areas must be colossal.

Blast Injuries

The first detailed histologic study of the effects on the central nervous system of blast from high explosive shells is found in a paper by Mott,[1] which comprises the Lettsonian Lectures delivered before the Medical Society in London in February and March, 1916. During the Civil War, Mitchell, Morehouse and Keen[2] described the blast syndrome in unmistakable terms, but the neuron at that time was not an entity, since staining of the nervous system to aid in histologic scrutiny had scarcely begun. Mott draws attention to Sir Anthony Bowlby's[3] Bradshaw Lecture, *Wounds in War*, delivered in 1915, in which he remarks:

> It must also be kept in mind that the mere explosive force of the gases of a large shell exercises great powers of destruction. The expansion of the gases is alone sufficient to kill, and in the only case in my experience in which an autopsy has been made, the brain was the seat of very numerous petechial haemorrhages.

This brain, which had been in Sir Arthur Keith's custody, was turned over in 1916 to Mott, who confirmed the existence of widespread petechial hemorrhage, but who also noted changes compatible with carbon monoxide poisoning. He cites, in addition, several nonfatal cases in which the explosion of large shells caused loss of consciousness without visible external signs of injury. In all these cases, the patient in question was propelled some distance by the blast wave, but there were no external injuries to suggest a primary blow on the head. Two of these cases may be cited:

> A lieutenant under my care told me that he was in a communication trench when an aerial torpedo exploded close to him. He felt a great pressure against him; it was soft but sufficiently powerful to knock him down unconscious. He did not know how long he was unconscious, but thinks it must have been an hour. When he recovered consciousness he got up and was helped away. His head felt as if it would burst, and ever since he has had a whizzing in the left ear and dizziness. Dreams of bombs and aerial torpedoes bursting. There was no parapet to blow down on him.
>
> An R.A.M.C. officer at the battle of Ypres had a shell explode near him. He was not hit, but lay unconscious for six hours. He recollects the shock of the shell as he went out of the dressing-room. For some days he suffered with severe headache and soreness of back of head and down the spine; the lower extremities felt heavy, but there was no loss of feeling. He had retention of urine for a day only, and around the body there was a pain like an appendix pain. He rapidly recovered.

The first case is typical of hundreds of thousands in World War I. One must recall that men were engaged in trench warfare, and that they were protected from shell fragments by being submerged in trenches but were not protected from the blast wave of a shell exploding in close proximity. On recovery, those who were actually rendered unconscious by proximity to an exploding shell complained of headache, dizziness, lethargy and inability to concentrate — in short, they exhibited all the major signs and symptoms of the postconcussion syndrome of peacetime. In the parlance of the early days of the last war, they were said to be suffering from "shell shock" (von Sarbó[4]).

The problem of distinguishing psychogenic war neurosis from a case of organic concussion resulting from blast is delicate and often difficult, but I agree with Myers[5] that such a distinction is clearly essential. In a book recently published, he distinguishes between "shell concussion," a syndrome associated with organic injury to the brain, and "shell shock," a psychogenic syndrome due to the fears and fatigue of warfare. Often, however, the two syndromes are confused (Roubinovitch[6]).

It is interesting to trace the term "shell shock" in the various connotations that it acquired during World War I. Late in 1914 and during 1915, a soldier was said to have suffered shell shock when he was picked up unconscious and externally uninjured in the vicinity of an exploded shell. The usage was thus synonymous with "shell concussion." Stevenson,[7] however, in a short paper concerning the cause of death due to high-explosive shells in unwounded men, concluded that sudden death in these circumstances results from "concussion of the brain and interference with the functions of nerve centres which are essential to life, and the interruption of which means instant death." "I have seen many men," he continued, "home from the front who have been exposed to these explosions; all their symptoms and all their accounts of their experiences tend to confirm this belief, for it is to

the less severe injuries to these centres that the symptoms of men who recover and come home all point." Later, shell shock came to be applied more particularly to the cases of functional war neurosis.

Stevenson also refers to the interesting speculation of the French civil engineer, Arnoux,[8] who observed an exploded aneroid in the pocket of a French officer who had been killed by proximity to an exploding shell. The aneroid was repaired, and it was found that a sudden compression of 10,000 kilos per square meter was essential to disrupt it. Arnoux put forward the theory that, following such compression, gases in the blood and tissues expanded with bubble formation, and that men were killed by sudden massive air embolism. The aneroid observation is interesting, but the attempt to explain death as due to bubble formation was far fetched, since it did not take into consideration the rate at which gases dissolve under pressure, and the slow rate at which resolution occurs when pressure is diminished.[9]

To Mott[1] must be given the credit for having first emphasized the significance and likelihood of carbon monoxide poisoning in the vicinity of an exploding shell, especially one exploding in a confined space. Oxygen is absorbed by the explosion, carbon monoxide is liberated, and many of the so-called "deaths from blast" have been shown to be due to carbon monoxide poisoning of persons unconscious or pinioned under debris. The importance of carbon monoxide poisoning has lately been re-emphasized in connection with bombing injuries among civilians in England and Germany. However this may be, death from primary blast is a clinical entity that requires close study, because of its intimate connection with concussion and with the postconcussion syndrome of neuropsychiatry.

The general subject of blast injuries is discussed under four headings: the physics of the blast wave, the effects of blast on animals, the effects of blast on man, and suggestions concerning therapy.

Physics of Blast Wave

Bernal,[10] of Cambridge, England, has given the best general account of the physical characteristics of a high-explosive wave. In material of high density and small elasticity, the wave travels slowly; where density is small and elasticity great, as in air, the wave travels at great speed. The high pressures created by bomb explosions cause an enormous velocity of wave transmission in air, but the rate of movement diminishes rapidly as the wave proceeds and there is also a marked change in the shape of the wave as it progresses. The pressure in some waves rises immediately to its peak and then falls off gradually and is followed by a phase of less than atmospheric pressure, that is, the negative phase (Fig. 1). The generation of this steep-fronted wave is very similar to that of the waves that break on the seashore. The high-pressure phase of the disturbance, which always travels faster than the low-pressure phase, gets to the front just as the top of a wave on the sea, being held back less than the base by the friction of the sand, moves forward and ultimately breaks the wave.

This steep-fronted wave, sometimes known as the "shock wave," is responsible for blast and also for some of the bizarre effects of high explosives, such as the smashing of windows and doors at a

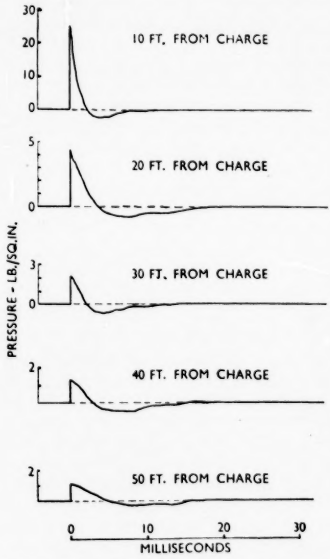

FIGURE 1. *Figures Showing the Progress of a Blast Wave from a Small Charge of Powder (Bernal[10]).*

distance. Pressure values of 5 to 10 pounds per square inch will break most windows, but blast pressures must rise to 6 atmospheres, or 100 pounds per square inch, before endangering a human being. This means that, to be injured by primary blast, a human being must be very near the site of the explosion. Zuckerman's[11] data on animals suggest that, at a distance of 30 feet from a 50-kilo bomb, a human being would be entirely safe from the direct effects of blast; published data concerning individual bombing episodes in which blast injuries have occurred in man support this deduction. With the large bombs, such as the 250-kilo and 500-kilo ones, the blast wave is more intense and travels farther.

Another aspect of bomb explosion concerns the blast wave in the earth, the so-called "ground

shock." Dropped from a great height, bombs generally penetrate some distance into the earth, the depth varying with the character of the surface. As previously mentioned, a 50-kilo bomb makes a crater of 20 to 30 feet in a dirt road. The sequence of events has been diagrammatically indicated by Bernal[10] (Fig. 2). A ground wave

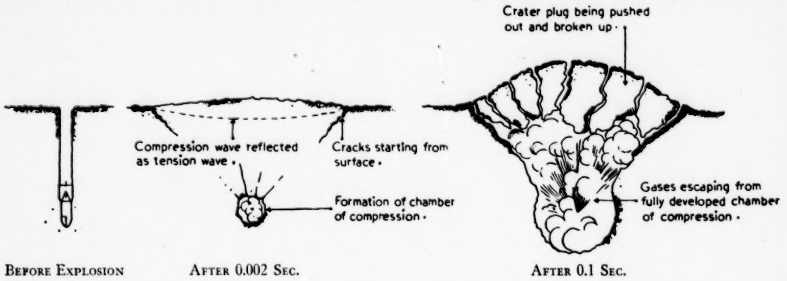
Crater plug being pushed out and broken up.
Compression wave reflected as tension wave.
Cracks starting from surface.
Formation of chamber of compression.
Gases escaping from fully developed chamber of compression.
Before Explosion
After 0.002 Sec.
After 0.1 Sec.

FIGURE 2. *The Series of Events Accompanying a Bomb Explosion in the Earth (Bernal[10]).*

has a high velocity, with an abruptly rising wave that may cause buildings to be shaken down at some distance from the site of the explosion.

Effects of Blast on Animals

The effects of primary air concussion due to shells or other explosives were not investigated experimentally until the end of World War I,[12-15] and to Hooker[16] must be given the credit for the most thorough experimental analysis as yet available. Men exposed to shell concussion, he pointed out, often developed a condition of shock that was unrelated to obvious trauma, since neither external nor internal wounds were clearly demonstrable. To investigate the phenomenon, a study was undertaken in the winter months of 1918-1919 at the Sandy Hook proving ground, with subsidy from the Committee on Shock of the National Research Council. In retrospect, it is highly significant and clearly a tribute to Hooker's insight that he regarded the condition of circulatory collapse following violent air concussion as indistinguishable from the circulatory collapse from primary shock that follows traumatic concussion in civil life. Hooker had opportunity to study the effects on frogs, cats and dogs, with the animals placed at varying distances from the muzzle of 10-inch and 12-inch guns and also from direct trinitrotoluene detonations. One dog, for example, placed 4 feet from the explosion of 4 pounds of trinitrotoluene, exhibited a fall in systolic blood pressure from 114 to 74 mm., and a fall in venous pressure from 8.7 to 6.2 mm. Hooker's studies emphasize four points: the fatal effects of primary blast occur in animals only relatively near the explosion, a difference of 2 or 3 feet often determining the question of life or death; there is a syndrome of primary shock characterized by collapse of the blood pressure in animals affected, but not killed, by the primary blast; there is complete absence of petechial hemorrhages or other intracranial lesions in the brains of animals exhibiting marked primary shock; and hemorrhagic lesions of the lungs and occasionally of other visceral organs are prevalent in animals subjected to blast. In his experience, however, the extent of the lung lesion bore little, if any, relation to the gravity of the concussion symptoms.

The experimental results of Hooker thus strongly suggest that the effects of primary blast in animals are closely similar to the effects of a blow on the head in an otherwise normal animal. He drew attention to the experimental studies of Githens and Meltzer,[17] and raised the question, without committing himself to an answer, whether the symptoms of air concussion were not ultimately similar to traumatic cerebral concussion.

Hooker's studies were published in 1924, but they aroused little comment. In the clinical literature during and after the war, there were many discussions of shell shock as an entity, and some authors, as already mentioned, used the term "shell concussion" to characterize symptoms resulting from primary blast.

New light on the problem has come from two groups of studies, one on blast and the other on experimental traumatic concussion of the head.

Primary blast. Zuckerman[11, 18] has given two detailed reports on the effects of primary blast in different animals, including mice, rats, guinea pigs, rabbits, cats, monkeys and pigeons. Seventy pounds of a high-explosive charge in paper containers so arranged that there would be no danger of injury from flying missiles was used as the source of the blast wave, and animals placed in well-anchored wire-mesh cages were arranged at

varying distances from the charge. As in the experiments of Hooker, there proved to be critical distance zones, which varied with the species of animal, monkeys being considerably more resistant, for example, than rabbits. No monkeys were killed by a 70-pound charge at distances greater than 18 feet, and in no animal, rabbits included, were effects detectable at distances greater than 50 feet, at which the positive component of the blast wave averaged 6.3 pounds per square inch. Between 13 and 18 feet, almost all animals were killed when so placed that their body walls were affected by hydrostatic pressure alone. At these distances, the positive component of the blast wave, that is, the hydrostatic pressure, varied between 126 and 63 pounds per square inch.

Between about 20 and 50 feet, no animals were killed, and those that survived showed little change in behavior. Those surviving between 18 and 21 feet often died within a few minutes to twenty-four hours after the blast; they exhibited widespread pathologic changes, the most conspicuous, as in Hooker's experiments, being hemorrhagic lesions of the lungs. But also, as in Hooker's experiment, there seemed to be no clear relation between the extent of the pulmonary lesions and the degree to which the animal had been affected by the blast wave. The pulmonary lesions are well illustrated in Zuckerman's[18, 19] later report.

Lesions were also found in other organs, including the epicardium of the heart, and very frequently in the large intestine, which proved to be the most susceptible, next to the lungs, to the effects of blast. The lungs, spleen and kidneys were often bruised or lacerated.

The nervous system was also carefully observed, especially in monkeys, the sections having been studied by Greenfield and also by Clark. The more important findings are summarized as follows[18]:

> No changes were observed in the cortex, mid-brain, pons or medulla of monkeys subjected to pressures as high as 110 lb. per square inch. On the other hand, most monkeys exposed to high pressures show extradural haemorrhages in the thoracic spinal roots, which are sometimes continuous with haemorrhage along the intercostal nerves. In two animals that died, haemorrhage had occurred at the central ends of the posterior columns, and in the dorsal commissure. Furthermore, most animals have shown a zone of oedema, absent in controls, around the central canal, especially in the thoracic region but also in the cervical and lumbar cord. This oedema may involve both anterior and posterior commissural fibres.
>
> Changes in nervous tissue are more pronounced in rabbits exposed to high pressures. Pial haemorrhages occur on the surface of the cortex, and haemorrhage from the tela chorcidea, filling the ventricles, has been observed. Haemorrhages have not been seen, however, in either the grey or white matter of the brain.
>
> Spinal-cord haemorrhages [in rabbits] are of the same kind as, but more severe than, [those] in the monkey.
>
> It is conceivable that as a result of these lesions the sympathetic outflow may be interrupted and that sensory defects may occur as a result of oedema and pressure on the commissures.

Stewart, Russel and Cone[20] report on injuries to the central nervous system of a pheasant by blast during an air raid. The blasted pheasant was found 90 feet from the edge of a bomb crater, dazed and paretic after two large bombs had been dropped, but there was no way of determining how near the bird had been to the actual site of the explosion. It was in a catatonic state, and tended to retain any attitude in which it was passively placed. Microscopic examination of the nervous system showed congested capillaries of the forebrain, associated with numerous petechial hemorrhages, which were most numerous in the hypothalamic area. There were also massive hemorrhages in both lungs and numerous small hemorrhages in the heart. The report of Stewart and his co-workers is essentially in harmony with that of Zuckerman for the more serious cases of blast injury, but Zuckerman and Hooker insist that conspicuous symptoms referable to the nervous system may often be found with little recognizable histologic change.

Concussion. In previous experiments on concussion, such as the excellent studies of Pilcher,[21] Schaller et al.[22] and Scott,[23] measured blows were delivered to an animal whose head was rigidly fixed; since anesthesia was employed, one criteria of concussion, namely, loss of consciousness, could not be appraised. The following clinical experience of Denny-Brown[24] suggested that acceleration of the head in space was essential for the concussion syndrome, rather than a blow on the head per se. An automobile mechanic, when his head was solidly on the concrete floor, had the misfortune to have a car fall off the jack, and his head was pinioned against the floor by the car's differential. He suffered a severe compound fracture, but no symptoms of concussion; indeed, immediately after the accident, the man was unaware that he was seriously injured. In this case, there had been no movement of the head, merely a crushing blow. Similar cases have just been reported by Eden and Turner.[25] If, however, the head is struck when unsupported and is thus able to move, symptoms of concussion inevitably develop. Furthermore, if the head, when moving, is brought abruptly to a stop, deacceleration occurs and is similarly effective in producing concussion. On the basis of this reasoning, Denny-Brown and Russell[24] devised a series of experiments in which a fixed head was struck with a pendulum moving

at velocities between 10 and 30 feet per second, the results being compared with those obtained with similar blows when the head was free to move. With the head fixed, blows that gave severe contusion and fractures of the skull failed to cause concussion. With the free head, three categories of symptoms developed, depending on the intensity of the blow, and usually appeared in the following sequence: shock, concussion and contusion.

Shock. When the blow is delivered at about 23 to 24 feet per second, the animal develops the classic symptoms of traumatic shock. The pulse rate slows for a time and then increases, the blood pressure falls, respirations become quick and shallow, and the animal becomes incapacitated for a period of several hours; but the knee jerks and the pinnal and corneal reflexes are unaffected. It is highly significant, especially in view of Hooker's[16] and Zuckerman's [18, 19] work on blast, that a blow on the head can of itself induce symptoms of generalized shock.

Concussion. A distinction is made between shock, as such, and symptoms of concussion, which develop when slightly heavier blows are delivered, that is, those struck at a velocity of 25 to 28 feet per second. Following these heavier blows, the corneal and pinnal reflexes are abolished for varying intervals, the resting posture (tonus) of the extensors disappears, and spinal reflexes may be altered or even temporarily abolished. A blow of this magnitude, if delivered to a conscious animal, renders it unconscious, whereas the blow causing shock does not necessarily cause unconsciousness.

The pathologic changes in the brain associated with shock and concussion blows have been carefully sought and have been proved wholly absent so far as ordinary microscopic examination is concerned. There are no petechial hemorrhages and no contused hemorrhagic areas in the medulla or cerebral hemispheres. The microscopic causes of the symptoms of concussion are still obscure, but no doubt they involve some basic intracellular disorganization of the neuron.

Contusion. When blows are delivered to the head at a rate greater than 28 feet per second, contusions usually develop in which hemorrhages occur beneath the site of the blow (or as a contrecoup at the opposite side of the head), and petechial hemorrhages are prone to develop, especially in the basal nuclei, brain stem and medulla. Age and other factors, however, affect the actual velocity essential for contusion.

The studies of Denny-Brown and Russell thus indicate that conspicuous concussion may be produced in animals without causing clearcut histologic changes. Studies of Hooker[16] and Zuckerman[11] prove that this is also true of blast concussion. Is there anything in common between direct traumatic concussion and blast concussion?

Zuckerman[18, 19] is of the opinion that lung damage is due to the physical impact of the blast wave against the thoracic wall rather than to sudden distention of the lungs by the positive component of the blast wave, or to a suction effect of the negative component of the blast wave. Such changes as occur in the central nervous system are likewise thought to be caused by sudden impact. There are obviously two components to be considered in the blast wave: the primary increase in atmospheric pressure to 100 pounds or more per square inch, and the rate of movement of the blast wave itself. Sudden increase of pressure might rupture the tympanic membrane, but from experience of caisson workers it is not likely that the pressure itself would cause concussion any more than a mechanical blow on a fixed head. A wave of moving pressure that gives acceleration of the body by virtue of its impact on the body wall—and hence imparts an acceleration to the body as a whole, including the head—reproduces in a very precise manner the type of acceleration or deacceleration known to be essential for the traumatic-concussion syndrome.

Those who are surprised by the apparent lack of histologic change in cases of concussion will be interested to learn that de Gutiérrez-Mahoney,[26] of Nashville, Tennessee, has confirmed the results of Denny-Brown and Russell, finding that when the fixed head is struck there is in fact no detectable histologic change, but that when the head is given an acceleration by a corresponding blow and concussion results, a widespread demyelinization of nerve tracts, followed by a transient appearance of fat droplets throughout the cerebral substance, can be detected; outspoken fat embolism may also result. The fat droplets and emboli tend to disappear entirely within three or four hours after the blow, and de Gutiérrez-Mahoney believes this to be the reason why fat embolism has not been previously demonstrated.

Fat embolism has assumed prominence in the present war, and there are many reports in the current literature, especially from England, concerning its incidence. In a group of 115 cases reported by Robb-Smith[27] in February, 1941, death was attributed to embolism in 25 per cent of cases. In a more recent discussion on fat embolism and the brain, Robb-Smith[28] and others who contributed to the discussion suggest that cerebral complications developing secondarily after an accident are due to the fat emboli that have passed through the lungs into the cerebral circulation. These may arise locally in contused tissues, such as a crushed long bone. Usually, the lungs separate out all the fat globules, but occasionally a pulmonary vein is torn so as to permit escape of fat into the systemic circulation. Robb-Smith states: "In systemic fat embolism the symptoms usually develop two to three days after the accident and are characterized first by delirium, which is frequently very violent, alternating with stupor which merges into coma. Localizing signs are usually absent or, if present, are chaotic. Hyperpyrexia is usual and it is not uncommon to find petechial haemorrhages in the skin of the neck, chest and arms, and their presence greatly facilitates diagnosis." He had not encountered cases in which cerebral fat embolism was attributable to direct traumatic concussion of the head.

Effects of Blast on Man

High-explosive bombs and shells have been used more widely on civilian populations and at sea during World War II than in any previous conflict. When bombs or shells explode in a confined space, as in a building or on a ship, the blast effects are many times intensified. There is thus no more urgent problem connected with the present war than the analysis of blast and its effect on the human body. Despite this, available literature is scant, and research endeavor has been limited to a small group of investigators in England, who took up the problem to help in designing adequate air-raid shelters for protection from blast,[29] as well as from high-velocity fragments. Although this country has for two years been aware of the bombing of cities and shelling of ships on the high seas, nothing has been done toward investigating blast.

From English sources, especially from the reports of Dean, Thomas and Allison,[30] Falla,[31] Hadfield and his co-workers,[32] Hadfield and Christie,[33] Kretzschmar,[34] Krohn,[35] Logan[36] and Thomson,[37] it is believed that death from uncomplicated primary blast in civilian areas is rare, but well-authenticated cases have been reported, especially in the recent and well-documented account of 17 cases by O'Reilly and Gloyne.[38] Uncomplicated cases of primary blast may, however, be relatively uncommon, since to be killed by its effects, the person must be very close to the explosion, that is, within 20 or 30 feet (50-kilo bomb). In these circumstances, the chances of being struck by the blast wave alone and not by splinters is somewhat remote. But there have been many thousands of cases in which primary blast and splinter injuries have coexisted. These have been especially common when a direct hit has been made on a crowded air-raid shelter. Similar episodes have occurred at sea, — in the shelling of crowded transports and warships, — and primary blast should therefore always be suspected in any bombing injury.

The histologic findings in man, so far as they have been described, are similar to those in Zuckerman's[18] monkeys subjected to blast waves of 100 pounds per square inch, namely, pulmonary hemorrhages, contusions and lacerations of other thoracic and abdominal viscera, minor changes in the central nervous system, and occasional areas of subpial hemorrhage.[38] Evidently, as in animals, profound concussion can occur with little in the way of histologic effect.[39] Whether acute cerebral fat embolism exists in such cases has not been determined.[40-42]

Therapy

It is not possible to discuss the difficult problems of therapy in cases of cerebral and pulmonary concussion resulting from primary blast, but one general principle is clear. As more is learned about traumatic concussion in civil life, as well as concussion from blast, it becomes obvious that anoxia plays a large role in the total picture. Blood pressure tends to fall as a result of primary shock.[24] The recent German literature[43] on cerebral blood flow following concussion, moreover, indicates that cerebral circulation becomes diminished, and that the pulmonary damage is frequently accompanied by fat embolism. All these circumstances, in my opinion, indicate the need for oxygen therapy, and for measures designed to improve the systemic and especially the cerebral circulation.[44]

References

1. Mott, F. W. The effects of high explosives upon the central nervous system. *Lancet* 1:331-338, 441-449 and 545-553, 1916.
2. Mitchell, S. W., Morehouse, G. R., and Keen, W. W., Jr. *Reflex Paralysis*. Circular No. 6, Surgeon General's Office, March 10, 1864. 17 pp. New Haven, Conn.: Yale University School of Medicine, 1941. *Gunshot Wounds and Other Injuries of Nerves*. 164 pp. Philadelphia: J. B. Lippincott and Co., 1864.
3. Bowlby, A. The Bradshaw lecture on wounds in war. *Lancet* 2:1385-1398, 1915.
4. von Sarbó, A. Die midrostrukturellen traumatischen Veränderungen des Nervensystems in Lichte der Kriegserfahrungen. *Schweiz. Arch. f. Neurol. u. Psychiat.* 29:127-152, 1932.
5. Myers, C. S. *Shell Shock in France 1914-18: Based on a war diary*. 146 pp. Cambridge University Press, 1940.
6. Roubinovitch, J. Les blessés de guerre sans blessures. *Bull. méd.*, Paris 54:65-67, 1940.
7. Stevenson, W. F. Note on the cause of death due to high-explosive shells in unwounded men. *Brit. M. J.* 2:450, 1915.
8. Arnoux [Cause of death from shell concussion]. *Le Journal*, Paris, July 6, 1915.
9. Pilcher, C. M. Results of projectile action. *History of the Great War. Medical Services. Surgery of the War* (Great Britain). 1:36-57, 1922.
10. Bernal, J. D. The physics of air raids. *Nature* 147:594-596, 1941.
11. Zuckerman, S. Experimental study of blast injuries to the lungs. *Lancet* 2:219-224, 1940.
12. Pitres, A., and Marchand, L. Quelques observations des syndromes commotionnels simulant des affections organiques du système nerveux central. *Rev. neurol.* 29²:298-311, 1916.
13. Marinesco, G. Lésions commotionnelles expérimentales. *Rev. neurol.* 31²:329-331, 1918.
14. Mairet, A., and Durante, G. Étude expérimentale de syndrome commotionnel. *Presse méd.* 25²:478, 1917. Contribution a l'étude expérimentale de lésions commotionnelles. *Rev. neurol.* 32:97-110, 1919.
15. Carver, A., and Dinsley, D. Some biological effects due to high explosives. *Brain* 42:113-129, 1919.
16. Hooker, D. R. Physiological effects of air concussion. *Am. J. Physiol.* 67:219-274, 1924.
17. Githens, T. S., and Meltzer, S. J. Phenomena following indirect concussion of the skull. *Am. J. Physiol.* 49:120, 1919.
18. Zuckerman, S. Discussion on the problem of blast injury. *Proc. Roy. Soc. Med.* 34:171-188, 1941.
19. *Idem*. Blast injury to lung. *Brit. M. J.* 1:645, 1941.
20. Stewart, O. W., Russel, C. K., and Cone, W. V. Injury to the central nervous system by blast: observations on a pheasant. *Lancet* 1:172-174, 1941.
21. Pilcher, C. Experimental cerebral trauma: the fluid content of the brain after trauma to the head. *Arch. Surg.* 35:512-527, 1937.
22. Schaller, W. F., Tamaki, K., and Newman, H. W. Petechial hemorrhages of brain experimentally produced in rats by concussion. *Arch. Neurol. and Psychiat.* 45:1-23, 1941.
23. Scott, W. W. Physiology of concussion. *Arch. Neurol. and Psychiat.* 43:270-283, 1940.
24. Denny-Brown, D., and Russell, W. R. Experimental cerebral concussion. *J. Physiol.* 99:153, 1940. Experimental cerebral concussion. *Brain* 64:93-164, 1941. Knock on the head. *Proc. Roy. Soc. Med.* 34:685, 1941. Denny-Brown, D. Delayed collapse after head injury. *Lancet* 1:371-375, 1941.
25. Eden, K., and Turner, J. W. A. Loss of consciousness in different types of head injury. *Proc. Roy. Soc. Med.* 34:685-691, 1941.
26. de Gutiérrez-Mahoney, W. The pathogenesis of traumatic unconsciousness: importance of fat embolism. *War Med.* 1:816-823, 1941.
27. Robb-Smith, A. H. T. Pulmonary fat-embolism. *Lancet* 1:135-141, 1941.
28. *Idem*. Discussion on fat embolism and the brain. *Proc. Roy. Soc. Med.* 34:639-642, 1941.
29. Barcroft, J. *Sectional Steel Shelters: Report upon investigation of the standard of protection afforded*. London: His Majesty's Stationery Office, 1939.
30. Dean, D. M., Thomas, A. R., and Allison, R. S. Effects of high-explosive blast on the lungs. *Lancet* 2:224-226, 1940.

31. Falla, S. T. Effect of explosion-blast on the lungs: report of a case. *Brit. M. J.* 2:255, 1940.
32. Hadfield, G., Ross, J. M., Swain, R. H. A., Drury-White, J. M., and Jordan, A. Blast from high explosive: preliminary report on ten fatal cases, with a note on the identification and estimation of carboxyhaemoglobin in formol-fixed material. *Lancet* 2:478-481, 1940.
33. Hadfield, G., and Christie, R. V. Case of pulmonary concussion ("blast") due to high explosive. *Brit. M. J.* 1:77-78, 1941.
34. Kretzschmar, C. H. Wounds of the chest treated by artificial pneumothorax. *Lancet* 1:832-834, 1940.
35. Krohn, P. L. Blast injury to lung. *Brit. M. J.* 1:645, 1941.
36. Logan, D. D. Detonation of high explosive in shell and bomb, and its effects. *Brit. M. J.* 2:864-866, 1939.
37. Thomson, F. G. Notes on penetrating chest wounds. *Brit. M. J.* 1:44-46 and 317, 1940.
38. O'Reilly, J. N., and Gloyne, S. R. Blast injury of the lungs. *Lancet* 2:423-428, 1941.
39. Fulton, J. F. Weir Mitchell Lecture. Neurology and war. *Tr. & Stud., Coll. Physicians, Phila.* 8:157-165, 1940.
40. Rehwald, E. Neurologisches Übersichtsreferat: Commotio und Contusio cerebri. *Med. Klin.* 36:867-869, 1940.
41. McKibben, P. S. A note on intravascular fat in relation to the experimental study of fat embolism in "shell shock." *Am. J. Physiol.* 48:331-339, 1919.
42. Rowlands, R. A., and Wakeley, C. P. G. Fat-embolism. *Lancet* 1:502-507, 1941.
43. Wanke, R. Zum Kreislaufgeschehen nach Hirnverletzung (Hirnverletzungsshock). *Arch. f. klin. Chir.* 200:189-201, 1940.
44. Davis, H. A. Physiologic effects of high concentrations of oxygen in experimental secondary shock. *Arch. Surg.* 43:1-13, 1941.

ENTEROCOCCAL ENDOCARDITIS*

Report of Two Cases

DAVID SKINNER, M.D.,† AND JESSE E. EDWARDS, M.D.‡

BOSTON

OF the various bacteria causing subacute bacterial endocarditis, the enterococcus is encountered infrequently. Since we have recently had the opportunity of observing 2 patients with enterococcal endocarditis, it is of interest to review each case and the literature, with particular reference to the pathology and bacteriology.

Thirty-seven cases of enterococcal endocarditis have been reported with varying degrees of completeness in the accessible literature,[1-28] and mention has been made of several more.[6, 29-40]

The clinical course of these cases is not pathognomonic of their etiology; it is indistinguishable from that of the common subacute bacterial endocarditis due to *Streptococcus viridans*. From the blood stream of each of the 37 patients discussed, enterococci were recovered on one or more occasions. The shortest known duration of one of these cases was six weeks, the longest thirteen months, and that of half the cases was between two and three months. Of the 25 patients whose underlying cardiac lesions were given on the basis of clinical or anatomic evidence, 20 had rheumatic, 4 had arteriosclerotic, and 1 had syphilitic valvular disease.

Autopsies were performed on 17 of these 37 patients. In all autopsied cases the clinical diagnosis of subacute bacterial endocarditis was substantiated. In general, the additional findings were the usual ones of multiple embolic phenomena. Five patients had cardiac lesions of special interest. Four had severe myocardial damage characterized by replacement of the muscle fibers by scar tissue.[3, 20, 23] The coronary artery of 1 of these 4 cases was involved in a mycotic aneurysm.[20] In the fifth patient, there was a small abscess in the myocardium.[16]

In 9 of the 17 cases in which autopsies were performed, an attempt was made to isolate the organism; in each, an enterococcus was cultured from the heart's blood or vegetations, or both. Smears or sections of the heart valves in 3 other cases disclosed gram-positive cocci in pairs and short chains. Enterococci were also recovered in cultures of various embolic abscesses in 5 of the cases.

The portal of entry of the infection was not discussed in 15 of the 37 cases. In 8, it could not be determined. The possible or probable portal of entry stated for the remainder was an infected finger in 1,[2] infected tonsils in 1,[21] the gall bladder in 2,[16, 20] the urinary tract in 2,[8, 9] septic abortion in 3,[10, 17, 20] and the gastrointestinal tract in five.[7, 11, 13, 15, 19] Each of the 2 patients in whom the portal of entry was the urinary tract had a proved enterococcal urinary-tract infection and a urethral stricture. Subsequent to surgical relief of the stricture, each patient developed enterococcal endocarditis. From the gall bladder of 1 of the 2 patients whose portal of entry was considered to be the biliary tract, enterococci were cultured at autopsy. Four of the 5 patients whose gastrointestinal tracts were involved had had acute gastroenteritis. In the fifth patient, autopsy disclosed ulcerations of the rectosigmoid. No bacteriologic studies of the possible portals of entry of the remaining cases were made.

Unfortunately, the characteristics of the organisms recovered were described in detail in so few cases that a comparison of the different strains is not possible. The antigenic properties of only one of the organisms were investigated.[28] It should be noted, however, that half the cases were re-

*From the Mallory Institute of Pathology, Boston City Hospital.

†Formerly, resident in bacteriology, Mallory Institute of Pathology, Boston City Hospital.

‡Formerly, first assistant in pathology, Mallory Institute of Pathology, Boston City Hospital.

ported prior to the publication of Lancefield's[41] methods of classification.

Case Reports

Case 1. A 72-year-old businessman presented himself on March 30, 1939, with the chief complaint of twice having passed blood at the end of urination.

The past history, which revealed that in 1915 he was refused life insurance because of a heart murmur, was otherwise noncontributory.

The patient was first seen in January, 1934, because he suffered a burning sensation in the rectum after defecation. There were no associated urinary symptoms. About 6 weeks later, he began to have a slight burning on urination and to feel "uncomfortable." There was diurnal frequency of five or six times and no nocturia. Physical examination revealed a slight, apical, systolic, cardiac murmur; a blood pressure of 200/90; and a moderately enlarged but soft prostate. Proctoscopy yielded negative results. Laboratory data disclosed an essentially normal urine and peripheral blood, a negative Wassermann reaction, and blood-sugar and nonprotein nitrogen levels within normal limits. Roentgenographic studies of the chest, gall bladder, gastrointestinal tract and kidneys were essentially negative.

Five years later, in March, 1939, the patient returned with the chief complaint of having twice passed approximately a tablespoonful of blood at the end of urinating clear, nonbloody urine. There was no associated pain or dysuria. The urinary stream had become somewhat smaller during the intervening 5 years.

Physical examination showed that the patient had gained considerably in weight and had developed a very obese abdomen. On rectal examination, the prostate was greatly enlarged but soft. There were old blood and smegma about the corona and a moderate balanitis. His physical condition otherwise was essentially normal, not having changed appreciably during the 5-year interval.

Laboratory examinations disclosed a hemoglobin level of 100 per cent and a red-cell count of 5,250,000. A catheter specimen of urine was essentially normal. The blood nonprotein nitrogen level was 46 mg. per 100 cc. An intravenous pyelogram showed normal function in each kidney and a large intravesicular prostate, with elevation of the ureteral orifices, and back pressure into the ureters.

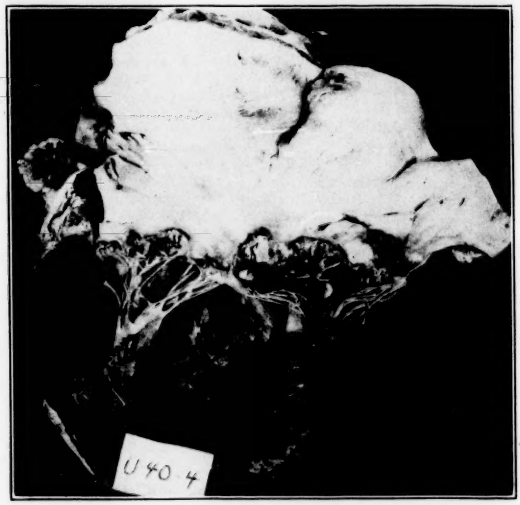

Figure 1.

Photograph of the mitral valve in Case 1, showing the fairly large, irregularly deposited vegetations of bacterial endocarditis.

On April 6, a bilateral vasotomy and a one-stage suprapubic prostatectomy were performed under spinal anesthesia. A very large, vascular prostate was enucleated by the usual technic. The bladder wall was greatly hypertrophied, and the histologic appearance of the prostate was that of benign enlargement. The patient had an uneventful convalescence.

Two months after the operation, in June, the patient began to exhibit an evening temperature of 100 to 102°F. Throughout the rest of the day, he felt well and at no time had chills. There occurred an occasional slight swelling of the right ankle, which was considered to be due to a mild pelvic phlebitis. However, the fever persisted, and, early in July, a blood culture grew an organism that morphologically resembled a pneumococcus.

The patient was again hospitalized. He had no complaints except the evening fever. His general physical condition was essentially as before. The prostatectomy wound was well healed, and the blood pressure was 140/80. Urinalyses showed only an occasional leukocyte

in the sediment. The hemoglobin level was 70 per cent, the red-cell count 3,000,000, and the white-cell count 14,000. The blood nonprotein nitrogen level was within normal limits. A roentgenogram of the chest taken with a portable machine showed a prominent heart shadow but otherwise was not remarkable. A blood culture taken on July 19 grew organisms that were similar in appearance to those previously recovered and were identified as enterococci. Three carious teeth were extracted. From their roots, the same organisms were cultured. Sulfapyridine was given empirically until a blood level of 11.5 mg. per 100 cc. was obtained. Because there was no amelioration of the fever and because the blood nonprotein nitrogen level reached 60 mg. 100 cc., the drug was withheld.

The patient was allowed to go home, where he continued to exhibit an evening temperature of 100 to 102°F. He gradually failed. On December 20, the blood hemoglobin, erythrocyte and leukocyte levels were within normal limits. Blood cultures taken on December 28 again grew enterococci. The patient died on January 4, 1940.

Autopsy. An autopsy was performed 12 hours post mortem. Only the pertinent findings are given.

The heart was of normal size, weighing 400 gm. The myocardium was firm and yellowish to deep red. In the lateral wall of the left ventricle approximately 2 cm. from the apex was a focus 1 cm. in diameter in which the myocardium was distinctly yellow. The foramen ovale, measuring 3 mm. in diameter, was anatomically though not functionally patent.

The mitral, aortic and tricuspid valves were the sites of a bacterial endocarditis, the lesions being much more extensive on the mitral than on the other valves (Fig. 1). On the mitral valve, the vegetations, measuring 5 mm. in thickness, were attached to the auricular surface of each cusp and extended slightly along the adjacent chordae tendineae. The surfaces of the vegetations were irregular, and their color varied from yellowish brown to gray. Although friable, they showed foci of calcification, especially in their basal portions. On and near the corpora arantii of the aortic valve were small, gray, friable vegetations, the aggregate measurement of those on each cusp being 4 by 3 by 2 mm. Along the line of closure of the tricuspid cusps was a row of noncontinuous, shallow ulcers measuring up to 8 mm. in diameter. Their bases were yellow and firm, suggesting calcification. The pulmonary valve was normal. None of the valves showed any evidence of disease preceding the bacterial endocarditis.

The aorta showed a moderate degree of atherosclerosis, with focal ulceration in the abdominal portion. In the right common and external iliac veins were small mural thrombi that appeared organized. These lesions were brownish-gray nodules measuring 4 mm. in diameter and did not appreciably narrow the lumens.

The spleen was moderately enlarged, weighing 500 gm. The capsular surface was smooth, glistening and purple except at one point situated at the junction of the diaphragmatic and gastric surfaces. Here was a depression measuring 1.0 by 0.8 by 0.5 cm. The tissues directly beneath this area for a depth of 5 mm. were firm and grayish yellow. Elsewhere, the cut surfaces were deep reddish purple and were studded with numerous bulging, translucent, semigelatinous nodules measuring up to 1 mm. in diameter.

The kidneys were of normal size, their combined weight being 300 gm. The capsules stripped with ease and revealed pale-gray, smooth surfaces on which were numerous linear and punctate red areas suggesting hemorrhages. Each cortex measured 5 mm. in thickness. On the pale-gray cut surfaces were punctate red areas.

The prostatic urethra was wide, measuring 1 cm. in diameter. It was walled by firm, fibrous prostatic tissue, which averaged 1 cm. in thickness and from which several gray nodules bulged above the cut surface. The seminal vesicles were slightly pale and thicker than usual.

The rectum contained a polyp measuring 1.0 by 0.8 by 0.5 cm.

Microscopic examination of the various tissues substantiated the anatomic findings. A section of the left ventricle taken through the yellow areas revealed scattered, small areas in which the muscle fibers had lost their nuclei and had developed a granular cytoplasm. In some places a small number of muscle fibers had disappeared, only stroma with dilated capillaries remaining.

The bacterial endocarditis appeared to be of longest duration on the mitral valve. A section of the cusp showed it to be thickened by fibrous tissue, infiltrated with lymphocytes, plasma cells and macrophages, and to have capillaries coursing through breaks in the elastica. On the auricular surface of the valve were several clumps of gram-positive diplococci partially covered with fibrin

FIGURE 2.

Photograph of the mitral vegetation in Case 1. Gram-positive cocci are present in clusters and suggestive chains (Gram–Weigert stain, × 1350).

(Fig. 2). In the underlying endocardium was young granulation tissue heavily infiltrated with neutrophilic leukocytes.

The section of the aortic valve showed a more recent and more acute lesion. Here was an ulceration extending through the entire thickness of the leaflet. At the margin of the ulcer were clumps of bacteria and organizing fibrin infiltrated with polymorphonuclear leukocytes. The fibrous thickening and vascularity seen in the mitral valve were absent.

The Malpighian corpuscles of the spleen contained a moderate amount of amyloid. Beneath the depression in the splenic capsule, the parenchyma was replaced by fibrous tissue infiltrated with a moderate number of lymphocytes, plasma cells and macrophages.

In the kidney, numerous glomerular spaces and adjacent tubular lumens contained fresh and old blood. There was no definite glomerular necrosis. The basement membranes of many glomerular tufts were thickened by a slight to moderate amount of amyloid.

The prostatic tissue showed moderate fibrosis but no evidence of active inflammation. However, the mucosa of the seminal vesicles was thickened by granulation tissue and contained small numbers of gram-positive diplococci. Within the lumens of the vesicles were polymor-

phonuclear leukocytes, lymphocytes and macrophages.

The rectal polyp was a typical benign polyp. At its base was an infiltration of a small number of neutrophilic leukocytes.

The final diagnoses were: subacute bacterial endocarditis, with extensive involvement of the mitral valve and slight involvement of the aortic and tricuspid valves; focal myocardial infarction; amyloidosis of the spleen, kidney and adrenal glands; healed infarct of the spleen; polyp of the rectum; old thrombophlebitis of the right common and external iliac veins; chronic seminal vesiculitis.

Case 2. A 60-year-old, Russian-Jewish painter was admitted to the hospital on July 12, 1939, with the chief complaint of difficulty in breathing, cough and intermittent pain in the chest increasing in severity during the preceding 4 weeks.

The past history was noncontributory.

In 1933, the patient first noted slight difficulty in breathing. Despite gradually increasing shortness of breath, he was able to continue work until March, 1936, when he was admitted to the hospital with the chief complaints of difficulty in breathing when prone and of swelling of the legs.

Physical examination at that time revealed a well-developed and well-nourished man experiencing slight dyspnea. Moist rales were heard in the posterior, basal portion of each lung field. The heart was enlarged to the left, and the heart sounds were of fair quality, without murmurs. The pulse was irregular, with a rate of 120. The blood pressure was 160/110. The lower border of the liver was palpated three fingerbreadths below the right costal margin in the right midclavicular line. Varicosities and marked pitting edema were present in both lower legs.

Laboratory data revealed a hemoglobin level of 85 per cent (Sahli), and a white-cell count of 5800. The blood nonprotein nitrogen level was 27 mg. per 100 cc. A blood Kahn reaction was negative. The urine was essentially normal. An electrocardiogram disclosed a ventricular rate of 85 and a QRS interval of 0.08 second; T_1 was upright, T_2 diphasic, and T_3 flat, and the axis was normal. These findings were interpreted as indicating auricular fibrillation and myocardial damage.

The patient responded favorably to the administration of digitalis and was discharged on the 13th hospital day. Thereafter, he continued to take digitalis and was able to work intermittently for about 2 years. During 1938, he found it necessary to restrict his activity because of progressive difficulty in breathing on exertion. About 3 months before his final admission to the hospital, he developed moderate difficulty in breathing when at rest, a moist, unproductive cough, with associated pain in the chest, intermittent swelling of the ankles and episodes characterized by hot and chilly sensations. For the week preceding entry, he felt especially "choked up."

Physical examination in July, 1939, revealed the patient to be orthopneic, cyanotic and in obvious respiratory distress, with a moist cough. The tongue was dry, and the teeth moderately carious. The pupils were irregular and slightly dilated, and reacted sluggishly to light. Ophthalmoscopic examination disclosed moderate tortuosity of the arteries and moderate venous congestion, with moderate arteriovenous nicking. There were bilateral pulsations at the root of the neck and moderate distention of the cervical veins. There were dullness, diminished breath sounds and rales at the bases of both lungs, and there was an area of dullness, with loud bronchial breathing and bronchophony, at the angle of the left scapula. The point of maximum cardiac impulse was at the left anterior axillary line in the 6th interspace, and the area of supracardiac dullness was increased in width. At the apex was a systolic thrill. A harsh, high-pitched systolic murmur was heard over the entire precordium and was loudest at the apex. There was a soft, blowing diastolic murmur at the mitral area and the right sternal angle, but it was loudest over the sternum. The pulmonic second sound was louder than the aortic. The cardiac rhythm was totally irregular, and the ventricular rate averaged 70. The blood pressure was 170/65. There was a right inguinal hernia. The area of hepatic dullness extended three fingerbreadths below the costal margin in the right midclavicular line. Rectal examination showed external hemorrhoids. There was moderate pitting edema of the lower legs. A vascular tumor was present on the right palm. The radial and brachial arteries were moderately thickened and tortuous. The reflexes were physiologic.

Laboratory data showed the urine to be acid and to have a specific gravity varying from 1.011 to 1.020. Albumin and sugar were constantly absent. The urinary sediment contained 0 to 5 leukocytes and 0 to 3 granular casts per high-power field. Hematologic studies showed a red-cell count of 4,100,000, a hemoglobin of 83 per cent (Sahli) and white-cell counts varying from 31,600 to 57,000. Differential leukocyte counts averaged 88 per cent neutrophils, 8 per cent monocytes and 4 per cent lymphocytes. A blood Hinton reaction was negative. Nonprotein nitrogen levels of 86 and 89 mg. per 100 cc. were obtained. Roentgenograms of the chest showed a general enlargement of the heart without increase in the size of the aorta, congestive changes in both lower lobes and a pneumonic process in both midlung fields. An electrocardiogram taken the day after admission disclosed auricular fibrillation, a ventricular rate of 95, a QRS interval of 0.07 second, T_1, T_2 and T_4 diphasic with low origin, T_3 inverted with low origin, and a normal axis. The interpretation was auricular fibrillation and myocardial damage. On the same day, the vital capacity was 2.2 liters, the circulation time 23 seconds, and the venous pressure in the left arm 7 cm. of water. A sputum culture grew a streptococcus with alpha hemolysis and *Staphylococcus aureus*. Seven daily blood cultures grew enterococci.

The patient's temperature rose to 101.1°F. on the 2nd day, dropped to normal for 4 days, and terminally rose to 100°F. The pulse rate averaged 88, except for a rise to 120 during the last 2 days. Similarly, the respiratory rate averaged 30, with a terminal rise to 52. Treatment consisted in venesection, with removal of 600 cc. of blood, digitalis, Mercupurine, aminophyllin and sulfapyridine. During the 2nd day, the patient developed a Cheyne–Stokes type of respiration, which continued intermittently thereafter. The cardiac sounds varied from a harsh, high-pitched, apical systolic murmur and a soft, blowing diastolic murmur to low-pitched, booming systolic and low-pitched diastolic murmurs. On several occasions, the diastolic murmurs were inaudible, and once a soft aortic diastolic murmur was heard. On the 3rd hospital day, petechiae were noted in the right conjunctiva and over the right upper arm. The patient failed to improve, developing on the 7th day a persistent Cheyne–Stokes type of respiration, increasing temperature and pulse rate, and rales. He died on the following day, July 20.

Autopsy. An autopsy was performed 12 hours post mortem. Only the important findings are given.

The heart was increased in size, weighing 500 gm. The myocardium of each ventricle was hypertrophied, the left measuring 2 cm. in thickness, and the right 8 mm. The coronary arteries showed a mild degree of athero-

sclerosis but no appreciable degree of narrowing of their lumens.

The mitral valve evinced a well-established rheumatic stenosis, the valve orifice being narrowed to a diameter of approximately 1 cm. On the auricular surfaces of the fused mitral cusps was a bulky vegetation. This was firmly attached to the endocardium and measured 2.3 cm. in width and 6 mm. in height. The remaining valves were normal.

In the cecum was a smooth-surfaced polyp measuring 8 mm. in diameter. Adjacent to this was an area of superficial ulceration with a dark, brownish-green base, measuring 4 cm. in greatest extent. The rectum showed some hemorrhoids.

The kidneys were reduced in size, their combined weight being 190 gm. The capsules stripped with ease, and the parenchymal surface was smooth except for an occasional linear scar 3 mm. or less in depth. On section, the cortex averaged 5 mm. in thickness and was pinkish red, with no evident hemorrhages.

Microscopic examination of the various tissues substantiated the anatomic findings. A section of the left ventricle revealed small foci in which the muscle fibers had disappeared; only stroma with dilated capillaries and scattered pigment-laden macrophages remained.

A section of the mitral valve disclosed an ulceration extending through the entire substance of the leaflet. The hiatus was filled by a vegetation composed of partially organized, old fibrin, erythrocytes, leukocytes and gram-positive cocci in pairs, short chains and clusters (Fig. 3). Beneath the ulcerated surfaces was young granulation tissue. In the substance of the leaflet remote from the ulceration were foci of necrosis and infiltration of moderate numbers of polymorphonuclear leukocytes.

FIGURE 3.

Photograph of the mitral vegetation in Case 2. Gram-positive cocci are present in clusters (Gram–Weigert stain, × 1350).

In the gastrointestinal tract were two lesions, one in the rectum, and one in the cecum. The section of the rectal lesion disclosed hemorrhoids of moderate size and also an acute inflammatory process in the mucosa. The lesion in the cecum was characterized by infarctlike necrosis, with ulceration and infiltration and a moderate number of neutrophils and many diplococci and bacilli. Cocci in pairs and short chains were the predominating organisms in the cecal wall.

The final diagnoses were: subacute bacterial endocarditis involving the mitral valve; old rheumatic heart disease, with mitral stenosis; myocardial hypertrophy; focal myocardial infarction; pulmonary congestion and edema; polyp and focal acute ulceration of the cecum; hemorrhoids.

BACTERIOLOGY

The organism of Case 1 (Strain A) was obtained in pure culture from four ante-mortem cultures, in conjunction with a *Str. viridans* from an extracted tooth, in pure culture from the heart's blood at autopsy, and in conjunction with a *Staph. albus* from the vegetation. The organism of Case 2 (Strain O) closely resembled that of Case 1. This strain was obtained in pure culture from six ante-mortem blood cultures and from another in conjunction with a *Staph. albus*. The post-mortem blood culture was negative. Cultures of the vegetation and an unorganized mural thrombus yielded the organism in pure culture.

On smear, the organisms are gram-positive, lanceolate diplococci, often appearing encapsulated, and arranged singly and in short chains. They grow well in broth, producing an even turbidity. On the surface of a blood-agar plate (20 per cent defibrinated sheep blood), they form discrete, small, grayish-white convex colonies, which produce a very faint zone of alpha hemolysis that is best seen after a colony is scraped aside. The organisms grow readily on the surface of 40 per cent bile agar and are insoluble in bile. They produce acid fermentation of dextrose, lactose, galactose, maltose, trehalose, salicin, sorbitol and mannitol, and split esculin. They do not ferment sucrose, arabinose, raffinose or inulin. The pH of dextrose broth is lowered from 7.0 to 4.3. Acid and a slight clot are formed in litmus milk. The two strains differ somewhat in their resistance to heat: Strain A resists a temperature of 60°C. for thirty minutes, whereas Strain O resists that temperature for ten minutes. Extracts of the organisms were tested for precipitin reactions with serums of Lancefield's Groups A to H streptococci, inclusive, and gave reactions with Group D antiserums. These two strains were found not to correspond with the few known serologic types within this group.

DISCUSSION

The term "enterococcus" is best used to denote a group of related organisms whose normal habitat is the intestinal tract. The enterococcus is described as a gram-positive, lanceolate diplococcus occurring in short chains.[29, 42–47] It is often somewhat pleomorphic and sometimes appears encapsulated. On the surface of blood agar, it grows well as a round, convex, lenticular, sharply contoured colony producing a slight amount of alpha hemolysis. It also grows well in broth or on agar containing 10 per cent, 20 per cent or 40 per cent bile, and is insoluble in bile. The organism is hardy, requiring infrequent transplanting, and

most strains resist a temperature of 60°C. for thirty minutes. Its biochemical activities include the formation of acid and a soft clot in litmus or methylene blue milk and the reduction of the pH of dextrose broth from 7.5 to 4.2. Acid without gas is produced in dextrose, lactose, sucrose, trehalose, salicin, mannitol and sorbitol, and inulin and raffinose are not fermented. Esculin is split. Antigenically, this group comprises Group D of Lancefield's classification.[37, 41, 46, 47]

Attempts at subdivision of the group on the basis of cultural and biochemical characteristics have resulted in considerable confusion. The American and English authors, exemplified by Sherman,[46] subdivide the enterococcus group into four closely related species, *Str. faecalis*, *Str. liquefaciens*, *Str. zymogenes* and *Str. durans*, of which the first is the type form. The more recent German authors, exemplified by Gundel,[48] divide the enterococci into Types A and B, of which Type B corresponds to the typical enterococcus and Type A exhibits less vigorous cultural and biochemical activities and less pathogenicity for mice than Type B. The development by Lancefield[41] of a practicable method of grouping streptococci on the basis of antigenic structure has already shown that many of the various species of enterococci belong to Group D.[47]

Comparison of the characteristics of the organisms recovered from these 2 cases with those of the type organism showed a striking similarity. In the tests used, Strain A reproduced the type reaction except for its failure to ferment sucrose. Similarly, Strain O differed from the type organism only in its failure to ferment sucrose and in its heat resistance. Despite these aberrations, it seems evident on the basis of cultural, biochemical and antigenic properties that these two organisms are enterococci.

Comment should also be made concerning the possible sources of entry of the enterococcus into the blood stream in these 2 cases. In Case 1, autopsy revealed two possible sources, the infected polyp of the colon and the seminal vesicles. The inflammatory lesion in the polyp was not extensive and undoubtedly originated at a later date than the endocarditis. On the other hand, the seminal vesicles evinced a long-standing inflammatory process and contained organisms morphologically similar to the enterococcus. These observations, together with the clinical history of the development of the endocarditis subsequent to the prostatectomy, imply but do not prove that the seminal vesiculitis was the portal of entry of the enterococcus. In Case 2, there were in the cecum and rectum moderately acute ulcerations heavily infiltrated with bacteria morphologically similar to enterococci. Although these ulcerations might constitute the portal of entry of the organism, the acuteness of the lesions probably indicates that they were of more recent origin than the endocarditis.

Two other observations deserve mention. In each case, throughout the myocardium, were focal areas in which the muscle fibers had disappeared, only the stroma remaining. Such lesions are consistent with those produced by arterial occlusion. Although no occlusions of the coronary arteries were demonstrated, it is reasonable to assume that some of the smaller branches of the arteries were obstructed, possibly by emboli.

The other and more unusual complication of bacterial endocarditis was amyloidosis. Deposits of amyloid were found in the spleen, adrenal gland and kidney in Case 1. An explanation of its occurrence here might lie in the long duration of the endocarditis.

Summary

Two cases of subacute bacterial endocarditis caused by an enterococcus are presented.

In Case 1, the symptoms of endocarditis appeared following a prostatectomy. The patient died seven months later. Necropsy showed typical vegetations involving the mitral, aortic and tricuspid valves, focal myocardial infarction, evidence of seminal vesiculitis of long duration and the unusual finding of amyloidosis. The organism (Strain A) was recovered from four ante-mortem blood cultures and an extracted tooth, and from the heart's blood and the vegetations at autopsy. There was no demonstrable underlying cardiac disease. The portal of entry may have been the infected seminal vesicles.

In Case 2, the symptoms of endocarditis appeared in a patient who had cardiac decompensation, which had progressed slowly throughout a six-year period. The duration of the endocarditis was probably about three months. Necropsy evinced old rheumatic heart disease, with involvement of the mitral valve, typical vegetations on that valve and focal myocardial infarction. Although fairly acute ulcerations of the rectum and sigmoid were found, these probably were of too recent occurrence to have been the portal of entry. The organism (Strain O) was recovered from seven ante-mortem blood cultures and from the vegetations and an unorganized mural thrombus at autopsy.

The characteristics of these organisms are those of an enterococcus, with the exceptions of the failure of both strains to ferment sucrose and the diminution of the heat resistance of Strain O. Both

strains are members of Group D (enterococcus) of Lancefield's classification of streptococci.

We are greatly indebted to Dr. A. R. Kimpton for permission to report Case 1 and to Dr. R. C. Lancefield for grouping and attempting to type the organisms.

References

1. MacCallum, W. G., and Hastings, T. W. A case of acute endocarditis caused by *Micrococcus zymogenes* (nov. spec.), with a description of the microorganism. *J. Exper. Med.* **4**:521-534, 1899.
2. Braxton-Hicks, J. A. An unusual organism (*Micrococcus zymogenes*) in a case of malignant endocarditis. *Proc. Roy. Soc. Med.* **5**: (path. sect.) 126-130, 1912.
3. Costa, S., and Boyer, L. Sur un microcoque isolé du sang, d'un épanchement articulare et d'un nodule sous-cutané au cours d'une endocardite infectieuse maligne à forme prolongée. *Compt. rend. Soc. de biol.* **88**:188-190, 1923.
4. Costa, S., and Boyer, L. Sur un microcoque isolé du sang au cours d'un deuxieme cas d'endocardite infectieuse à forme prolongée. *Compt. rend. Soc. de biol.* **88**:473, 1923.
5. Gallavardin, L., and Langeron, L. Endocardite infectieuse à entérocoque. *Lyon méd.* **132**:314-317, 1923.
6. Gundel, M., and Seeber, F. Die klinische Bedeutung der Enterokokken in Magen-Darmkanal. *Deutsches Arch. f. klin. Med.* **164**:190-201, 1929.
7. Rouslacroix, A., Zuccoli, and Martin, P. Endocardite maligne et septicémie à entérocoques. *Compt. rend. Soc. de biol.* **95**:499-502, 1926.
8. Meyer, K. Über Enterokokkensepsis. *Klin. Wchnschr.* **6**:2045-2047, 1927.
9. Fuss, E. M. Urogene Enterococcensepsis. *Med. Klin.* **23**:245, 1927.
10. Tidow, G. Enterokokkensepsis unter dem Bilde der Endocarditis lenta. *Med. klin.* **25**:872, 1929.
11. Duvernay and Gerbay. Entérococcie. Myocardite. Mort. *Lyon méd.* **143**:636-638, 1929.
12. Cade, A. Septicémie à entérocoques avec endocarditis à marche lente. *Lyon méd.* **143**:689-691, 1929.
13. Gundel, M. Bakteriologie und Klinik seltener Streptokokkeninfektionen. *Deutsches Arch. f. klin. Med.* **168**:129-155, 1930.
14. Rosenberg, G. Der Enterokokkus als Erreger von Endocarditis chronica. *Zentralbl. f. Bakt.* (Abt I) **121**:75-85, 1931.
15. Boyer, L., and Sauvan, A. Sur un germe du type entérocoque obtenu par hémoculture dans un cas d'endocardite maligne. *Compt. rend. Soc. de biol.* **108**:104-106, 1931.
16. Rosenberg, G. Zur Kenntnis der Enterokokken-Endokarditiden. *Klin. Wchnschr.* **11**:359-362, 1932.
17. Dumas, A., and Josserand, P. Endocardite infectieuse à entérocoque. (Retrécissement mitral antérieur. Evolution rapide après une fausse couche.) *Lyon méd.* **151**:637-643, 1933.
18. Cossio, P., Berconsky, I., and Fisher, A. Endocarditis infecciosa a enterococcos. *Semana méd.* **2**:1911-1914, 1933.
19. Grögler, F. Über Enterokokkenendokarditis. *Zentralbl. f. inn. Med.* **55**:689-693, 1934.
20. Wallach, K. Subacute enterococcus endocarditis. *J. Mt. Sinai Hosp.* **1**:80-83, 1934.
21. Baum, M. Ein Fall von Enterococcus-Endokarditis. *Wien. klin. Wchnschr.* **48**:1067-1069, 1935.
22. Reiners, H. Enterokokken-Endokarditis. *Klin. Wchnschr.* **15**:1067-1069, 1936.
23. Grögler, F. Neue Erfahrungen zur Frage der Enterokokkenendokarditis. *Deutsches Arch. f. klin. Med.* **180**:153-163, 1937.
24. Waaler, E. Bacterial endocarditis caused by hemolytic fecal streptococci (enterococci). *Acta med. Scandinav.* **91**:121-126, 1937.
25. Clements, A. B. Enterococcus endocarditis. *New York State J. Med.* **37**:1842-1844, 1937.
26. Otto, E. Beitrag zur Kenntnis der Enterokokkenendokarditis. *Klin. Wchnschr.* **17**:1847-1850, 1938.
27. Rohleder, T. Ein Beitrag zur Frage der Enterokokken-Endokarditis. *Monatschr. f. Kinderh.* **73**:361-366, 1938.
28. Williams, C. Bacterial endocarditis due to the *Streptococcus faecalis*: report of a case. *Am. Heart J.* **18**:753-758, 1939.
29. Andrewes, F. W., and Horder, T. J. A study of the streptococci pathogenic for man. *Lancet* **2**:708-713, 775-782 and 852-855, 1906.
30. Marchal, G., and Jaubert, A. Étude bacteriologique de l'endocardite infectieuse secondaire lente à streptocoques. *Presse méd.* **34**:324-327, 1926.
31. Ribeyro, R. E. Enterococemia. *Crón. méd., Lima* **44**:4-8, 1927.
32. Clerici, A. Endocardite infettiva da enterococco. *Gazz. d. osp.* **49**:353-355, 1928.
33. Wyss. Cited by Reiners.[22]
34. Halle, J., Girard and Odinet, J. Cited by Cossio, Berconsky and Fisher.[25]
35. Henske. cited by Reiners.[22]
36. Parenti, G. C. Endocardite da enterococco. *Sperimentale, Arch. di biol.* **88**:218-228, 1934.
37. Lancefield, R. C., and Hare, R. The serological differentiation of pathogenic and non-pathogenic strains of hemolytic streptococci from parturient women. *J. Exper. Med.* **61**:335-349, 1935.
38. Kolář, K. Immunotherapy in enterococcus septicemia and endocarditis. *Bratisl. lekár. listy* **16**:561-575, 1936.
39. Picard, J., and Marquet, G. Septicémie entérococcique maligne: endocardite, pleurésie séro-fibrineuse: modes d'action du carbone intraveineux. *Progrès méd.* pp. 862-868, 1936.
40. Duthoit, A., and Demarez, R. Deux cas de septicémie à entérocoques. *Echo méd. du Nord* **8**:773-780, 1937.
41. Lancefield, R. C. A serological differentiation of human and other groups of hemolytic streptococci. *J. Exper. Med.* **57**:571-595, 1933.
42. Topley, W. W. C., and Wilson, G. S. *The Principles of Bacteriology and Immunity.* Second edition. 1645 pp. Baltimore: Wm. Wood and Co., 1936. Pp. 453-458 and 468.
43. Dible, J. H. *A System of Bacteriology in Relation to Medicine.* Vol. II. 419 pp. London: His Majesty's Stationery Office, 1929. Pp. 124-136.
44. Kolle, W., Kraus, R., and Uhlenhuth, P. Enterococcus. In Kolle und Wasserman's *Handbuch der pathogenen Mikroorganismen.* Third edition. Vol. VI. Jena: Gustav Fischer; Berlin and Wien: Urban und Schwarzenberg, 1929. Pp. 399-402.
45. Dible, J. H. The enterococcus and the faecal streptococci: their properties and relations. *J. Path. & Bact.* **24**:3-35, 1921.
46. Sherman, J. M. The streptococci. *Bact. Rev.* **1**:3-97, 1937.
47. Smith, F. R., and Sherman, J. M. The hemolytic streptococci of human feces. *J. Infect. Dis.* **62**:186-189, 1938.
48. Gundel, M. Das biologische System der Streptokokken. *Zentralbl. f. Bakteriol.* (Abt I) **115**:44-66, 1929.

LEFT INGUINAL HERNIA WITH ACUTE MECKEL'S DIVERTICULITIS AND PERITONITIS

Report of a Case

ROLF LIUM, M.D.,* AND SAMUEL T. LADD, M.D.*

PORTSMOUTH, NEW HAMPSHIRE

WHEN acute inflammation of Meckel's diverticulum is encountered at operation, it is usually recognized by the surgeon. We wish to report a case in which Meckel's diverticulitis complicated a strangulated left inguinal hernia. The diagnosis was not apparent until the patient had left the hospital and a considerable amount of detective effort had been expended.

CASE REPORT

A 75-year-old, Irish-born, retired machinist was admitted to the Portsmouth Hospital on February 12, 1941. It was impossible to obtain an accurate detailed history from him because of mental confusion. The first symptom was generalized abdominal pain, which began 2 weeks before admission. There had been some retching at the onset, but no vomiting. The patient had not noted any distention of the abdomen, nor did he describe the abdominal pain as crampy. During the 2 weeks before admission, he felt a steady "soreness across the abdomen," and was unable to eat. The bowels moved without cathartics about once in three days. The last bowel movement was on the day of admission. There was no blood or mucus in the stools.

For the previous 2 years, the patient had noted gradually developing symptoms of prostatism. His urinary stream had become smaller, there was increasing difficulty in starting the urine, and he had nocturia of two to five times. At no time had he seen blood or pus in the urine. The patient had noted some dyspnea on exertion during the preceding 6 months, but no edema or paroxysmal nocturnal dyspnea. He had some orthopnea and used two pillows at night. The family and marital histories were noncontributory. The patient had used alcohol quite freely until 2 years before admission, when he had stopped suddenly at the direction of his physician.

Physical examination showed a well-developed and well-nourished man with respirations of 30 and signs of dehydration. His pulse was completely irregular, with a radial pulse deficit of 15 beats. There were many coarse rales throughout the lungs, but no area of consolidation was found. The abdomen was soft and not distended; it was tender throughout, the maximum tenderness being over a mass in the left groin. This mass was firm and rounded, measured 4 cm. in diameter, and was not reducible. It lay just above the center of Poupart's ligament. The blood pressure was 130/70. There were 4 or 5 white blood cells per high-power field in the urine, but no albumin or sugar. The white-cell count was 29,000, with 89 per cent polymorphonuclear leukocytes. The temperature was 102°F. orally.

Four cat units of Digifolin were given intramuscularly, an intravenous injection of 10 per cent glucose in physiologic saline was begun, and the operation on the mass in the left lower quadrant was undertaken with local anesthesia. The preoperative diagnosis was strangulated inguinal hernia, with a question of Richter's hernia.

The peritoneum was entered at a point above the hernia, and the sac opened from above. The neck was very narrow and consisted of a thick fibrous band. There was free, seropurulent fluid in the abdominal cavity, with large flakes of fibrin. The loops of sigmoid and small intestine were bound together with fine adhesions. The posterior wall of the sac was composed of a 4-cm. long, acutely inflamed tip of what appeared to be an appendix and its mesentery (Fig. 1). The organ was visualized 4 cm. above the tip, in the medial direction, and this portion seemed to lie entirely in the retroperitoneal area. Further exposure was not possible without extension of the incision.

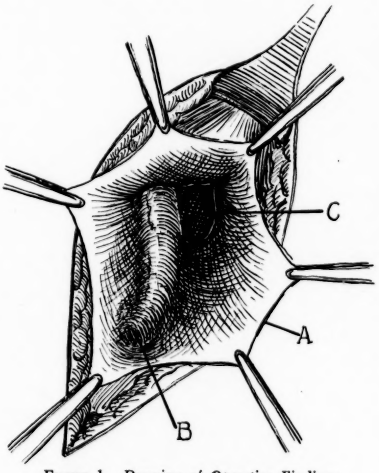

FIGURE 1. *Drawing of Operative Findings.*
A — *cut edge of hernial sac;* B — *acutely inflamed tip of Meckel's diverticulum;* C — *cut edge of neck.*

In view of the patient's general condition, the simplest procedure was adopted: the inflamed tip was amputated, and the sac removed with it en masse. When the peritoneum was closed, it was necessary to overlap the edges somewhat so as not to incorporate the stump in the suture line.

The hernia was repaired with catgut, the second method of Halsted being used. The cord was left in its bed; the cremaster muscle was imbricated beneath the conjoined tendon and the conjoined tendon beneath the lower leaf of external oblique muscle, with the leaves of the

*Surgeon, Portsmouth Hospital.

external oblique muscle overlapped. A drain was left in the lower angle of the wound. The report of Dr. H. N. Kingsford on the specimen was as follows:

> The specimen consists of a sac, open at one end. It reveals a projection into its lumen measuring 4 by 1 cm. Sections show a peritoneal covering, subperitoneal tissue and two smooth-muscle layers, with a marked purulent exudate on the lumen edge of the section; there is absolutely no evidence of mucosa. This could be a Meckel's diverticulum or an appendix.

The convalescence was complicated by bronchopneumonia on the 2nd postoperative day; this was controlled by sulfathiazole. On the same day, the patient developed acute urinary retention, which necessitated an indwelling catheter. He was digitalized by the 3rd day, and from then on ran a regular pulse. The gastrointestinal tract revealed its functional integrity soon after operation by the passage of flatus, which continued to occur without abdominal discomfort. Sepsis developed in the wound, but 5 weeks after operation there was only a small sinus and no evidence that the hernia was recurring. The patient had recovered sufficiently 2 weeks after operation to undergo a transurethral resection for benign prostatic hypertrophy.

With the available evidence, it seemed that we had been dealing with an acute appendicitis and peritonitis in a left inguinal hernia. However, a barium enema done postoperatively showed the cecum in the right lower quadrant, with the appendix well outlined for a length of 10 cm. It was freely movable and showed no evidence of attachment to the site of the hernial sac. Previous to prostatectomy, a cystogram gave no indication of a bladder diverticulum. A gastrointestinal series six weeks after operation showed a loop of small bowel, about 30 cm. above the ileocecal valve, close to the anterior abdominal wall in the left lower quadrant and apparently attached in this position (Fig. 2).

In the last analysis, it seems that the diagnosis was acute Meckel's diverticulitis in a left inguinal hernia, with perforation and peritonitis, and not acute appendicitis, as we suspected at first.

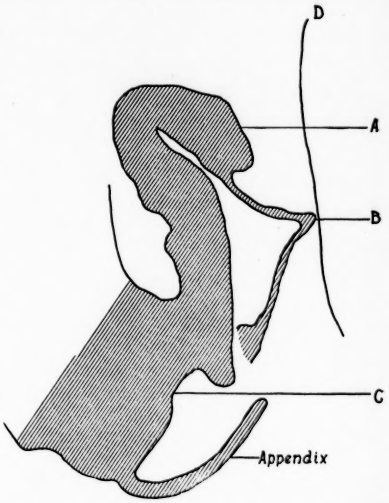

FIGURE 2. *Tracing of X-ray Plate Six Hours after a Barium Meal.*

A — terminal ileum; B — point of fixation to site of hernial sac; C — cecum; D — line of abdominal wall.

IRRADIATION IN THE TREATMENT OF CANCER OF THE BREAST*

FREDERICK W. O'BRIEN, M.D.,† AND EUGENE McDONALD, M.D.‡

BOSTON

A DISCUSSION of the place of irradiation in the treatment of mammary cancer naturally divides itself into an attempt to evaluate the usefulness of the procedure in primary operable cases, as the sole therapeutic measure; as a preoperative procedure; as a postoperative routine; in the control of local recurrences and distant metastases; and in cases with frankly inoperable tumors.

The radiation method is based on the object of treatment, — namely, cure or palliation, — the physical setup — namely, adequate amounts of radium and roentgen-ray apparatus of accepted potential — and the experience of the radiologist. Because of the nature of this presentation, a detailed statistical analysis is not attempted.

Irradiation Alone in Operable Cases

Irradiation as the sole therapeutic measure is justifiable in cases, otherwise operable, in which the patient is a poor surgical risk, in the borderline operable patient and in specially organized clinics.

Since 1922, Keynes[1] has treated 390 selected cases of operable cancer of the breast with buried radium needles. He does not recommend their use in very advanced stages of breast cancer, cases with demonstrable distant metastases, avascular ulcerated tumors or very stout patients, since a great deal of fat in the breast and axilla makes accurate placing of the needles difficult. He considers all other cases suitable, and believes that patients in the very earliest stage of the disease are eminently suitable for radium treatment. He shows a five-year survival rate of 65.9 per cent, and he states that it is certain that many of the patients included in his Class I cases (with disease apparently confined to the breast) should really appear in Class II, that is, among those with metastatic involvement of the axillary glands. This fact suggests that if a correction for this error could be made, the statistical result in Class I would be very much better than it actually appears to be. Keynes sometimes removes the breast by diathermy. It must be remembered that his radium attack is a highly individualized surgical procedure.

We are not aware that anyone has systematically treated primary operable breast cancer with x-rays alone, except when for some reason surgical intervention has been contraindicated, and even these cases do not run into numbers comparable with those of Keynes.

We do not believe, other things being equal, that irradiation to the exclusion of surgery should be employed in that group of patients with mammary cancers who, when operated on radically, give a five-year cure rate (alive without disease) of 70 per cent or better, as reported by Simmons and his associates.[2] It may be argued that this is a rigidly selected group, but that is as it should be. From our experience, it seems the part of wisdom to drop the term "operable breast cancer" and use the designation "curable cancer." The surgeon who thinks in terms of curable cancer is very much less likely to intervene in a case that is technically operable but in which operation would shorten the patient's life.

The extent of the disease, here as elsewhere, has come to be recognized as the most vital single factor influencing cure. Once the disease has extended to the axilla, the five-year cure rate by surgery drops to about 30 per cent. Less emphasis is placed on the grading of malignant tumors than formerly, for it has been shown that, regardless of the grade, if the tumor is localized and removed in its entirety, the cure rate is not affected. The grade of malignancy has, however, a prognostic value. Tumors of high malignancy are commoner in the younger age groups and are likelier to have already metastasized. These cases, for the most part, prevent a perfect surgical cure rate.

Preoperative Irradiation

The foregoing suggests the advisability of preoperative x-ray or radium therapy, not to supplant surgery but to complement it. Much of the criticism of preoperative irradiation has been justified. We do not believe that an inoperable cancer is made operable in the sense of curability by irradiation, but we do believe that the attempt should be made to immobilize tumors of high malignancy by judicious preoperative irradiation in an attempt to improve the cure rate of this group. And this can be done without prejudice to rather prompt surgical intervention.

The objections commonly raised against preoperative irradiation are that delay in operating creates a mental and physical hazard for the patient, and that adequate irradiation produces fibrosis, and makes the operation more difficult and the skin less likely to heal. Furthermore, if the

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 22, 1941.

†Chief, Tumor Clinic, Boston City Hospital.

‡Resident in radiology, Boston City Hospital.

tumor disappears under irradiation, the patient may be falsely misled into not returning for surgery; and, finally, there is no evidence to prove that preoperative irradiation is of benefit.

The last objection will always remain imposing and difficult to refute while surgeons hold out steadfastly against trial of the method. If patients are seen privately or in a tumor clinic and assured that the irradiation is in preparation for surgical excision later, no mental hazard need exist; the physical hazard already exists. If the disease has already extended to the axilla and beyond at the time of the first examination, it is difficult to reason that immediate irradiation will stimulate the spread of the disease rather than immobilize what is already there. There is no scientific evidence that irradiation stimulates tumor growth; on the contrary, there is abundant animal and human evidence that it halts neoplastic growth.

The method of administering preoperative irradiation, both the total dosage and the chronologic spacing of the unit dose, is of the greatest moment. The work of Adair and his associates[3] is frequently quoted in disparagement of preoperative irradiation. We agree that if one were to follow literally the method employed by Adair, one would have to expect the untoward results described by him. But it should be recalled that he intentionally used large doses of intensive radiation to obtain data on the cancerocidal effects of x-rays on the tumor in the breast and axillary nodes.

We do not believe that radiation in amounts sufficient to sterilize the tumor is either desirable or necessary after massive doses of x-radiation. Melnick and Bachem,[4] working with transplantable rat tumors, observed necrosis of tumor cells, hyperemia, cellular infiltration, granulation-tissue proliferation, fibrosis and blood-vessel changes, whereas after fractional and protracted methods of irradiation, only the most radiosensitive cells were destroyed by necrosis, the remaining resistant cells being transformed into tumor giant cells that degenerated not by necrosis but by calcium deposit, with no apparent effect in adjacent normal tissues. Melnick[5] repeated the experiments, using radon implants, with results parallel to those of the earlier study. In view of the experimental findings in animal tumors, Halley and Melnick[6] now prescribe preoperative irradiation extending over four or five weeks and followed by amputation within two to four weeks. A shorter preoperative course fails to obtain optimum tumor damage. The mutationlike effects, which they believe may be the most significant mechanism, require four to five weeks. Surgery done within two or three weeks of the end of irradiation has the advantage of dealing with a tissue in which viable tumor cells have been decreased to a numerical minimum, with slight damage to the tumor bed. Delay of surgical interference beyond four weeks, according to Halley and Melnick, makes regrowth of the tumor probable. Optimum spacing of the radiation dose may well be the crux of the entire problem, as indicated in the work of Spear and Glücksmann.[7]

Postoperative Irradiation

Routine postoperative irradiation has been abandoned in some clinics because of apparently paradoxical results, and carried on in others in the belief that the question is still *sub judice*. We are convinced that if postoperative irradiation is to be given in its commonly accepted sense of "prophylactic," many more fields of irradiation should be utilized than is the prevailing custom, as suggested by Lenz et al.[8] It is not sufficient to treat the affected chest wall, axilla and supraclavicular chain of lymphatics; one must treat the mediastinum and parasternal nodes, as well as the lymphatics of the opposite breast, over a protracted period.

We do not believe, however, that postoperative irradiation is necessary in those patients in whom the disease was localized in the breast by diagnostic roentgen-ray, operative and pathological examinations, with the exception of Grade III tumors, which are presumed to metastasize early. Roentgen-ray castration may be of value.

On the other hand, we are of the opinion that postoperative irradiation is definitely a useful therapeutic measure in patients whose disease appeared localized in the breast clinically but on pathological examination was found to have extended to the axillary nodes. In one series examined by us, 39 per cent of patients so classified lived over five years without demonstrable disease.

By far the largest group referred to our clinic for postoperative irradiation is made up of patients in whom the operation was frankly inadequate or of doubtful completeness. Irradiation of this group is usually only palliative, and is given with the idea of growth restraint and in the hope that if the remaining cancer cells are implanted elsewhere they may be less viable. Sometimes, physicians are critical of irradiation because it does not compensate in some miraculous way for lack of surgical judgment. Indeed, the radiation therapist has been accused of venality[9] when he treats these cases, whereas his confrere is pardoned for having operated on them. In our series of 50 consecutive cases of this type, 29 patients had surgery only and lived on the average nine months, whereas 21 who had surgery and irradiation lived

on the average over three years. Not a single patient in the first group lived five years, but in the latter group 5 lived for more than five years.

In 1940, a monograph[10] covering the treatment of cancer of the breast quoted, in censure of postoperative irradiation, statistics from a paper that appeared in 1935 based on cases operated on and irradiated from 1910 to 1929— a period when radiation therapy had hardly reached its adolescence. Many clinics during this time were treating patients with apparatus of diagnostic potential only. We believe that statistical data founded on radiation methods abandoned for more than a decade should be presented merely for what they are worth.

It should be plain that end results bear a direct relation to the criteria of operability, the extent of the disease, the degree of malignancy, the pathological interpretation, the kind of operation done, the skill of the operator and the use of any supplemental measure, such as radiation.

It is one thing to compare surgical end results in cases free of axillary nodes with similar cases that have had radiation added; it is another matter when axillary nodes or other complications are present. It is necessary to know how many patients had surgery only in the presence of skin ulceration, cutaneous nodules, supraclavicular nodes, distant metastases, secondary radical procedures, inflammatory carcinoma and lactating breasts; how many had surgery and irradiation; and when irradiation was given in relation to the operation. Much of the criticism leveled at radiation therapy is vitiated by failure to apply the principle that only like things are comparabie.

Irradiation for Local Recurrences and Distant Metastases

Local recurrence in the skin or scar, when the nodules are discrete and few in number, may be excised surgically or treated by surface or interstitial radium or intensive x-radiation with a well-localized field. If the nodules are multiple and contiguous, surgical removal is not usually advisable because of the loss of skin entailed thereby. In this situation, high-voltage x-rays or radium when available in sufficient quantity is preferable.

The appearance of secondary nodules in the scar or skin of the breast area usually means that the extirpation of the mammary gland was not wide enough. Hicken[11] has shown by mammographic studies that the lactiferous ducts spread over the entire anterolateral wall of the chest. Examining breasts supposed to have been completely excised by "mastectomy procedures" after injection of the ducts with a solution of methylene blue, he did not find a single case in which the mammary tissue had been removed in its entirety. In 94 per cent of the cases, the dye escaped in the subareolar zone, indicating that some of the breast had been left attached to the reflected skin flaps.

In an earlier study of 255 cases of breast cancer, one of us (F. W. O'B.[12]) found recurrence in the skin or scar in 21 per cent of the cases. The appearance time of the local recurrence in this group seemed directly related to the completeness of the surgical excision and the extent of the disease at the time of operation, rather than to the kind of tumor.

Distant metastases, on the other hand, involve other factors than completeness of operation and extent of the disease. They occur when, according to the rules of the game, they should not. In such cases, the kind of tumor and its method of spread by the lymphatics or vertebral veins seem of significance. The estrogenic theory of multiple foci of origin must also be considered when one discusses what seems to be a metastasis but what in reality may be one of several primary foci.

Often enough, metastases that are presumed to be postoperative were present at the time of surgical intervention. It is safe to assume that bone metastasis demonstrable by x-ray study ten days after operation has been present for a much longer period. In the records of more than 50 per cent of one series examined by us, there was no evidence of preoperative diagnostic x-ray examination. Roentgenologic study of the chest, spine and pelvis should be made before operation, as White[13] counsels, without regard to the smallness of the primary tumor, lack of nodes or suggestive symptoms. When this procedure is employed, many cancers clinically localized prove to be diffuse and inoperable.

Distant metastases may be controlled for long periods by appropriate gamma radiation or high-voltage x-rays. In suspected bone metastasis, irradiation should be promptly directed to the site of pain irrespective of negative diagnostic x-ray examination. The entire vertebral column may be riddled with tumor, without demonstrable roentgenologic findings. Any orthopedic appliance used in the presence of collapse of the vertebral bodies or fracture of the long bones that will preclude irradiation, since new-bone formation often enough follows its application, should be interdicted. Occasionally, generalized skeletal

metastases have disappeared completely following irradiation of the ovaries.

Pleural effusion sometimes resolves after relatively small doses of medium-voltage x-ray therapy, and the progress of lung metastasis is halted by fibrosis deliberately produced by the employment of supervoltage radiation. Such therapy is palliative, to be sure, but it is comparable in some measure with therapeusis in certain other chronic but fatal maladies common to the field of internal medicine.

Irradiation of Inoperable Tumors

The inoperable cases are cheerfully passed on to the radiation therapist. Although such cases are hopeless as a group, enough palliative benefit ensues to justify acceptance of such patients when they are not in extremis. Ulcerating breasts frequently heal, axillary and supraclavicular nodes regress, but secondary deposits appear in the skeleton or other organs. Care should be exercised that these patients have proper medical follow-up. A judicious use of sedatives, antianemic remedies and relatively small doses of radiation help a few to live in comparative comfort for five years or longer.

* * *

In conclusion, we do not claim that irradiation is in competition with surgery. We wholeheartedly subscribe to the dictum that any surgeon who does less than a radical operation in curable breast cancer is not giving his patient even a sporting chance for recovery. Likewise, we believe that the surgeon who studiously condemns irradiation on statistical data derived from cases treated just after the turn of the century, when the limits of surgical curability were ill defined and radiation therapy was still undeveloped, denies to his patient a therapeutic aid to longer life.

References

1. Keynes, G. The place of radium in the treatment of cancer of the breast. *Ann. Surg.* **106**:619-630, 1937.
2. Simmons, C. C., Taylor, G. W., and Welch, C. E. Carcinoma of the breast. *Surg., Gynec. & Obst.* **69**:171-177, 1939.
3. Adair, F. E. The effect of preoperative irradiation in primary operable cancer of the breast. *Am. J. Roentgenol.* **35**:359-370, 1936.
4. Melnick, P. J., and Bachem, A. The time factor in the irradiation of malignant tumors. *Arch. Path.* **23**:757-792, 1937.
5. Melnick, P. J. Unpublished data.
6. Halley, E. P., and Melnick, P. J. Preoperative irradiation in carcinoma of the breast. *Radiology* **35**:430-438, 1940.
7. Spear, F. G., and Glücksmann, A. The effect of gamma radiation on cells *in vivo*. *Brit. J. Radiol.* **14**:65-76, 1941.
8. Lenz, M., Frantz, V. K., and Kasabach, H. H. Prophylactic postoperative roentgentherapy for carcinoma of the breast. *New York State J. Med.* **34**:881-887, 1934.
9. Wolfer, J. A. Book review. *Treatment of Cancer and Allied Diseases. Surg., Gynec. & Obst.* **71**:534, 1940.
10. Pack, G. T., and Livingston, E. M. *Treatment of Cancer and Allied Diseases.* 1500 pp. Vol. 1. New York and London: Paul B. Hoeber, Inc., 1940.
11. Hicken, N. F. Mastectomy: a clinical pathologic study demonstrating why most mastectomies result in incomplete removal of the mammary gland. *Arch. Surg.* **40**:6-14, 1940.
12. O'Brien, F. W. Skin metastasis in post-operative irradiated breast cancer. *Radiology* **30**:437, 1938.
13. White, W. C. Irradiation as an aid to surgical treatment of cancer of the breast. *J. A. M. A.* **110**:261-265, 1938.

MEDICAL PROGRESS

MEDICAL ASPECTS OF OBSTETRICS

JUDSON A. SMITH, M.D.*

BOSTON

OF THE medical complications of pregnancy, the most important are those conditions characterized by hypertension and albuminuria and often loosely grouped under the old-fashioned and misleading designation "toxemias of pregnancy." In 1940, the American Committee on Maternal Welfare adopted a classification of these toxemias that now seems to be gaining acceptance by obstetric clinics throughout the country. It was presented with a detailed explanation in a recent paper by Mussey and Hunt[1] and is given below in a slightly condensed form.

GROUP A. Diseases not peculiar to pregnancy.
- I. Hypertensive disease (hypertensive cardiovascular disease).
  - *a.* Benign (essential).
  - *b.* Malignant.
- II. Renal Disease.
  - *a.* Chronic vascular nephritis or nephrosclerosis.
  - *b.* Glomerulonephritis.
  - *c.* Nephrosis.
  - *d.* Other renal disease (such as pyelonephritis).

GROUP B. Disease dependent on, or peculiar to, pregnancy.
- I. Pre-eclampsia.
  - *a.* Mild.
  - *b.* Severe.
- II. Eclampsia.
  - *a.* Convulsive.
  - *b.* Nonconvulsive (that is, with coma and post-mortem findings typical of eclampsia).

This classification is entirely logical in theory, if one accepts the underlying assumption that there is a specific hypertensive disease peculiar to pregnancy. Group A is composed of cardiovascular and renal diseases that occur independently of pregnancy and whose association with pregnancy is therefore a matter of chance. Group B consists of a single disease, which is in some way caused by pregnancy and which is referred to as pre-eclampsia or eclampsia according to the severity of the symptoms. The persistent belief that eclampsia is a pathologic entity has rested mainly on three facts: it occurs in women who have never previously shown evidence of cardiovascular or renal disease; it not infrequently results in complete recovery, leaving no demonstrable evidence of impairment of the cardiovascular system or kidney; and its typical picture has not been observed apart from pregnancy.

The actual classification of individual cases according to the above scheme, at least during pregnancy, is often difficult or impossible, largely because there is no readily available diagnostic test by which pre-eclampsia can be recognized. We are forced to rely on two empirical facts: eclampsia rarely, if ever, occurs before the sixth lunar month, and pre-existing vascular or renal disease is usually definitely aggravated by the pregnancy before the sixth month. The twenty-fourth week, therefore, is arbitrarily taken as a dividing line. Hypertension appearing before that time is regarded as prima-facie evidence of a pre-existing disease independent of the pregnancy; hypertension appearing after the twenty-fourth week in a woman who has no history of vascular or renal disease is regarded as prima-facie evidence of pre-eclampsia. These criteria, of course, are not perfectly satisfactory. If, for example, a patient with pre-existing mild vascular hypertension becomes worse later in pregnancy, it is difficult to decide whether the original disease is aggravated or she is beginning to develop superimposed pre-eclampsia. Furthermore, in cases of mild hypertension appearing soon after the twenty-fourth week and remaining mild, it is usually impossible to determine whether the condition is delayed aggravation of a pre-existing vascular or renal disease or a mild subacute pre-eclampsia. As a practical rule in the management of these cases, however, it is always safer to regard acute exacerbations of hypertension or albuminuria as indicative of pre-eclampsia.

The distribution of these conditions, when classified as above, is shown in Table 1, which is taken from a recent study by Irving[2] of 1182 consecutive cases of hypertension and albuminuria in pregnancy.

During the past year, Smith, Smith and Schiller[3] have made an extremely interesting and valuable contribution to the study of the etiology of pre-eclampsia. They measured the levels of pregnanediol, estradiol, estrone and estriol and the es-

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. $4.00).

*Instructor in obstetrics, Harvard Medical School; assistant obstetrician, Boston Lying-in Hospital; obstetrician, Massachusetts General Hospital.

trogenic potency after hydrogenation in the urines of 22 patients with pre-eclampsia and eclampsia and of 15 normal women during the last trimester. The results indicated that pre-eclampsia is associated with a progressive deficiency of progestin, which results in a greater and more rapid destruction of estrogens. They consider this derangement of estrogen metabolism to be due to disturbed placental function, which, they point out, might result from numerous mechanical or organic interferences with placental blood supply. Their ideas of the relation between the changed estrogen metabolism and symptoms of pre-eclampsia are best expressed in their own words:

TABLE 1. *Diagnosis in 1182 Consecutive Cases of Hypertension and Albuminuria in Pregnancy.*

DIAGNOSIS	NO. OF CASES	PER CENT
Essential hypertension	68	5.8
Chronic renal disease	13	1.1
Pre-eclampsia, mild	889	75.0
Pre-eclampsia, severe (including 13 cases of eclampsia)	212	18.1

> We are convinced that the significant finding, so far as the clinical manifestations of pre-eclampsia and eclampsia are concerned, is the sudden, rapid destruction of estrogens. The menstrual phenomenon has also been found to be accompanied by the same evidence for rapid destruction of the estrogens following estrogen and progestin withdrawal. Furthermore, there is a striking similarity between the local changes in the premenstrual endometrium and the generalized disturbances so characteristic of pre-eclampsia and eclampsia. The menstrual discharge has been found to contain a potent toxin to the action of which we would attribute the local changes resulting in menstruation. The formation of this toxin appears to be closely allied to rapid destruction of the estrogens. By analogy, we would postulate that the same shift of steroid metabolism in pregnancy results in the formation, on a larger scale, of a similar toxin, possibly in the decidua. The albuminuria of pre-eclampsia might be ascribed to the effect of such a toxin acting on the kidney glomeruli, the hypertension to an actual Goldblatt phenomenon from renal arteriolar constriction due to the same toxin, and edema to an effect upon capillaries similar to that which takes place in the premenstrual endometrium.

Having arrived at these admittedly speculative conclusions, they tested them by treating a small series of patients with pre-eclampsia with daily injections of estrogen and progestin. The resulting shift toward normal in both the clinical manifestations and the hormonal changes was considered sufficient to bear out their theory. The authors noted, however, that the difficulty and expense of giving adequate daily doses of these hormones, for the present at least, preclude their use as a practical therapeutic measure.

Some newer methods of studying renal function have revived interest in this aspect of the hypertensive complications of late pregnancy. The phenolphthalein excretion, concentration test and urea clearance are usually normal in both essential hypertension and pre-eclampsia. When, however, the renal blood flow per unit of time and the filtration fraction are determined, certain deviations from normal appear.

By the filtration fraction is meant the proportion of plasma that is filtered through the walls of the glomerular capillaries into Bowman's capsule—that is, the ratio of the amount of the glomerular filtrate during a certain time to the amount of plasma that flowed through the kidneys during the same period. To determine the plasma flow, use is made of the fact that Diodrast, at low concentration in the plasma, has a renal-excretion ratio of very nearly 100 per cent. In other words, of all the Diodrast carried to the kidney by the renal artery, none escapes by the renal vein. Thus, measurement of the plasma level of Diodrast and of the amount excreted per minute permits calculation of the amount of plasma that has flowed through the kidneys. The volume of the glomerular filtrate can be measured simultaneously by determining the ratio of the quantity of inulin excreted each minute to the plasma level of inulin, since inulin is neither excreted nor absorbed by the cells of the tubules. The normal filtration ratio is about 0.20.

Corcoran and Page[4] have studied a series of late toxemias of pregnancy by these methods and report that there are three groups. In Group I, the plasma flow was diminished, and the filtration fraction was increased. These findings are consistent with constricted efferent arterioles and normal capillaries, and are characteristic of essential hypertension in the nonpregnant woman. The patients in this group presented the clinical picture of pre-existing or latent essential hypertension. In Group II, the filtration fraction was low, and the clinical picture was that of severe pre-eclampsia or eclampsia. Corcoran and Page suggest that a lowered filtration fraction is the physiologic manifestation of the swelling of the basement membrane of the glomerular capillaries, which is generally regarded as the characteristic renal lesion of pre-eclampsia and eclampsia. In Group III, the filtration fraction was normal, and the clinical manifestations were mild. The authors do not attempt to classify these cases but believe that many of them represent mild pre-eclampsia.

Chesley[5] has reported similar findings and has come to similar conclusions. He believes that the lowered filtration fraction indicates severe glomerular damage, and suggests that, if pre-eclampsia or eclampsia is a cause of subsequent hypertension, the patients with a marked lowering of the filtration fraction should show a high incidence of hypertension later. In his series of 10 cases, 4 pa-

tients were hypertensive — that is, they had blood pressures above 140 systolic, 90 diastolic — two years later. He also reports observations on 7 patients with normal blood pressure one to four years after severe pre-eclampsia or eclampsia. In several cases, there was a marked deficit in renal blood flow, and in 2 cases a marked lowering of the filtration fraction. Chesley suggests that in some of these cases, in spite of the absence of hypertension, there may be glomerular damage.

The frequency with which a so-called "toxemic" pregnancy is followed by essential hypertension or chronic cardiovascular disease has been repeatedly pointed out in the last few years. The most recent contribution of this sort is a statistical study by Peckham[6] of 500 such patients observed throughout pregnancy and subsequently followed from two to ten years. For inclusion in this group, it was required that the patient should have made a minimum of three visits to the clinic, at each of which the blood pressure and urine were normal. This resulted in the selection of a group of patients none of whom showed evidence of toxemia before the fourth lunar month. Of the entire group, 63 per cent were found to have chronic vascular damage. The series was divided first according to the month of onset of toxemia and then according to the time elapsed between the onset and delivery. It was found that the incidence of permanent damage was greater the earlier the onset and the longer the time between onset and delivery. Peckham believes the latter factor to be the more significant in prognosis and suggests that four weeks should be the maximum period of observation of the toxemic patient, ignoring, apparently, the problem of the viability or nonviability of the fetus. A complete discussion of these statistics is impossible, but attention must be directed to one point concerning the apparent effect of long duration of the toxemia, namely, that the longer the time elapsed between the onset of toxemic symptoms and delivery, the likelier it is that the clinical picture was the type to suggest latent pre-existing vascular disease rather than pre-eclampsia.

There has been no progress in the therapy of the toxemias of pregnancy. Goethals[7] last year discussed the treatment of eclampsia with veratrum viride, as reported by Bryant and Fleming.[8] If there have been any further reports of the use of this drug they have escaped my notice. Nicodemus[9] describes the treatment of 13 eclamptic patients with the oxygen tent; all recovered. Although this result is of no statistical significance, the idea seems, a priori, to be worthy of trial.

Numerous reports[10–18] have recently been published that add to the evidence of the effectiveness of Vitamin K in preventing hemorrhagic disease of the newborn. The ideal method of prophylaxis seems to be the parenteral administration of Vitamin K to the mother at the onset of labor and to the infant immediately after birth. There can no longer be any excuse for neglecting this precaution. Javert and Macri[19] present some evidence suggesting that the daily ingestion of mineral oil leads to a deficiency of Vitamin K in pregnant women by preventing absorption.

There is nothing to be added to the chemotherapy of puerperal sepsis except the introduction of a new analogue of sulfanilamide, namely, sulfadiazine. Long,[20] who has made a preliminary report on this drug, finds that it is somewhat less rapidly absorbed from the gastrointestinal tract than sulfanilamide, sulfapyridine and sulfathiazole, and that it is somewhat less rapidly excreted than sulfanilamide or sulfapyridine, when renal function is normal. It is relatively easy to maintain an adequate concentration of the drug in the blood, and as a matter of fact, the blood level must be followed carefully to prevent unnecessarily high concentrations. It produces very little nausea and vomiting and appears to be less apt to cause drug fever and drug rash than sulfanilamide, sulfapyridine and sulfathiazole. Up to the time of his report, Long had observed no cases of renal injury. Its effectiveness in hemolytic streptococcus infections compares favorably with that of sulfanilamide. As yet, there has not been sufficient experience with sulfadiazine to make its evaluation possible.

Heckel[21] discusses the possibility that chemotherapy during pregnancy and the puerperium may injure the fetus in utero or the nursing infant. He considers injury to the nursing infant from sulfanilamide extremely unlikely. This drug is excreted in the milk in a concentration approximating that in the blood. A nursing infant consequently can get only a minute dose from its mother's milk. Babies nursed by mothers receiving 4 gm. a day showed only traces of the drug in the blood and behaved quite normally. Injury to the fetus is theoretically possible, since there is evidence that the concentration of sulfanilamide in the fetal blood is equal to that in the mother's within a few hours after administration. Heckel reports results in 13 women who were given chemotherapy at various stages of pregnancy and followed through delivery. Twelve of the infants were normal. One infant had a moderately severe anemia, for which no cause could be found. Heckel suggests that the anemia might have been due to the sulfanilamide administered to the mother: she had received daily doses (maximum, 30 gr.) to a total of about 750 gr. over a period of thirty-seven days, terminating fifteen days before delivery. Whatever the chances of injury to the fetus may be, they are no greater, he believes, with large doses than with small ones.

Steiner and Lushbaugh[22] believe that they have

recognized a new obstetric disease. They report 8 cases of unexpected and rather sudden maternal death during labor or soon after delivery. Clinically, the symptoms were those of severe shock. In some cases, there was atony of the uterus and post-partum hemorrhage, but only after the appearance of shock. In some cases, there was acute pulmonary edema. The essential pathologic condition was found on microscopic examination to be widespread embolism of small pulmonary arteries, arterioles and capillaries by the particulate matter found in amniotic fluid and by meconium. They have duplicated the disease clinically and pathologically in rabbits and dogs by the intravenous injection of human amniotic fluid and meconium. Three of their cases were found at the Chicago Lying-in Hospital over a period of nine years, during which time there were 24,200 deliveries, an incidence of 1 in about 8000 deliveries.

Some recent discoveries in connection with intragroup transfusion reactions are of great interest to obstetricians. The subject of isoimmunization in relation to intragroup reactions has been completely presented in a progress report by Hooker.[23] The facts that are of interest to the obstetrician concern the atypical agglutinogen, which has been named the Rh factor (because it occurs in the blood of the *Macacus rhesus* monkey) and which is present in the red cells of about 86 per cent of human bloods.[24] Persons who have this factor in their red cells are Rh+; the 14 per cent of persons who lack it are Rh–. Since the Rh factor is inherited according to the Mendelian law as a dominant,[25] the children of an Rh– mother and an Rh+ father will all be Rh+ if the father is homozygous with respect to this factor. If the father is heterozygous with respect to the Rh factor, half the children will be Rh+. The frequency of such marriages (Rh– wife, Rh+ husband), if due to chance alone, should obviously be about 12 in 100. There is now convincing evidence[26, 27] that sometimes when an Rh– woman is carrying an Rh+ fetus in her uterus, Rh antigen from the fetal blood gains access to the maternal blood and stimulates the production of antibodies; the maternal antibodies readily diffuse into the fetal circulation, destroying fetal red cells and producing the disease known as erythroblastosis foetalis. From these facts, it is apparent that if the mother of an erythroblastotic child is transfused with blood from her Rh+ husband or from *any other Rh+ donor*, there is grave danger of a reaction. A number of such reactions have been reported — some fatal.[27] It must be borne in mind that this is an intragroup reaction — ordinary direct cross-matching of bloods will not detect the incompatibility. It can be detected, however, by incubating a mixture of recipient's serum and donor's cells at 37°C. for thirty minutes.[28] This precaution (incubation) in cross-matching, therefore, becomes imperative in the selection of donors for all pregnant and parous women. If incompatibility is found, it will be necessary to determine at once the Rh status of the woman. If she is Rh– and her blood contains anti-Rh antibodies, she can be safely transfused only from a donor in the correct blood group who is also Rh–. Since finding such a donor might take some time, maternity clinics should have lists of donors whose Rh status has been determined. It is well to remember, if one is in a hurry for an Rh– donor, that since the character of being Rh– is a recessive, a brother or sister of the Rh– patient is much likelier to be Rh– than a donor selected at random.

264 Beacon Street

References

1. Mussey, R. D., and Hunt, A. B. The toxemias of pregnancy and the management of parturition. *J. A. M. A.* **117**:1309-1313, 1941.
2. Irving, I. C. A study of consecutive cases of hypertension and albuminuria in pregnancy. *Pennsylvania M. J.* **44**:557-562, 1941.
3. Smith, O. W., Smith, G. V., and Schiller, Sara. Estrogen and progestin metabolism in pregnancy. *J. Clin. Endocrinol.* **1**:461-476, 1941.
4. Corcoran, A. C., and Page, I. H. Renal function in late toxemia of pregnancy. *Am. J. M. Sc.* **201**:385-396, 1941.
5. Chesley, L. C. The question of glomerular damage following toxemia of pregnancy. *Am. J. Obst. & Gynec.* **42**:229-235, 1941.
6. Peckham, C. H. Time of onset and duration of the toxemias of late pregnancy in relation to the development of permanent vascular damage. *Am. J. Obst. & Gynec.* **42**:638-645, 1941.
7. Goethals, T. R. Medical aspects of obstetrics. *New Eng. J. Med.* **224**:200-204, 1941.
8. Bryant, R. D., and Fleming, J. G. Veratrum viride in the treatment of eclampsia. *J. A. M. A.* **115**:1333-1339, 1940.
9. Nicodemus, R. E. Oxygen tent therapy in the treatment of eclampsia. *J. A. M. A.* **117**:1238, 1941.
10. McCready, R. L., Callahan, E. T., and Grandin, D. J. Parenteral vitamin K therapy in ante-partum women and its effects on the infants' prothrombin level. *Am. J. Obst. & Gynec.* **42**:398-404, 1941.
11. Javert, C. T., and Macri, C. Prothrombin concentration in normal pregnancy. *Am. J. Obst. & Gynec.* **42**:415-419, 1941.
12. Andrus, W. DeW. The newer knowledge of vitamin K. *Bull. N. Y. Acad. Med.* **17**:116-134, 1941.
13. Maumenee, A. E., Hellman, L. M., and Shettles, L. B. Factors producing plasma prothrombin in the newborn infant. IV. The effect of antenatal administration of vitamin K on the incidence of retinal hemorrhage in the newborn. *Bull. Johns Hopkins Hosp.* **68**:158-168, 1941.
14. Bohlender, G. P., Rosenbaum, W. M., and Sage, E. C. Antepartum use of vitamin K in the prevention of prothrombin deficiency in the newborn. *J. A. M. A.* **116**:1763-1766, 1941.
15. Huber, C. P., and Shrader, J. C. Blood prothrombin levels in the newborn. *Am. J. Obst. & Gynec.* **41**:566-574, 1941.
16. Mull, J. W., Bill, A. H., and Skrowronska, H. Effect on the newborn of vitamin K administered to mothers in labor. *J. Lab. & Clin. Med.* **26**:1305-1309, 1941.
17. Beck, A. C., Taylor, E. S., and Colburn, R. F. Vitamin K administered to the mother during labor as a prophylaxis against hemorrhage in the newborn infant. *Am. J. Obst. & Gynec.* **41**:765-775, 1941.
18. Edsall, G. The prothrombin level in early infancy: its relation to hemorrhage and other neonatal disturbances. *New Eng. J. Med.* **224**:762-766, 1941.
19. Javert, C. T., and Macri, C. Prothrombin concentration and mineral oil. *Am. J. Obst. & Gynec.* **42**:409-414, 1941.
20. Long, P. H. Sulfadiazine. *J. A. M. A.* **116**:2399, 1941.
21. Heckel, G. P. Chemotherapy during pregnancy. *J. A. M. A.* **117**:1314-1316, 1941.
22. Steiner, P. E., and Lushbaugh, C. C. Maternal pulmonary embolism by amniotic fluid: as a cause of obstetric shock and unexpected deaths in obstetrics. *J. A. M. A.* **117**:1245-1254 and 1340-1345, 1941.
23. Hooker, S. B. Isoimmunization in relation to intragroup hemolytic transfusion reactions. *New Eng. J. Med.* **225**:871-877, 1941.
24. Landsteiner, K., and Wiener, A. S. An agglutinable factor in human blood recognized by immune sera for rhesus blood. *Proc. Soc. Exper. Biol. & Med.* **43**:223, 1940.
25. Landsteiner, K., and Wiener, A. S. Studies on an agglutinogen (Rh) in human blood reacting with anti-rhesus sera and with human isoantibodies. *J. Exper. Med.* **74**:309-320, 1941.
26. Levine, P., Katzin, E. M., and Burnham, L. Isoimmunization in pregnancy. *J. A. M. A.* **116**:825-827, 1941.
27. Burnham, L. The common etiology of erythroblastosis and transfusion accidents in pregnancy. *Am. J. Obst. & Gynec.* **42**:389-397, 1941.
28. Levine, P. The role of iso-immunization in transfusion accidents in pregnancy and in erythroblastosis fetalis. *Am. J. Obst. & Gynec.* **42**:165, 1941.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28011

PRESENTATION OF CASE

A sixty-three-year-old housewife, formerly a factory worker, was admitted to the hospital because of jaundice, malaise, nausea, vomiting, weakness and abdominal discomfort.

She had been in excellent health until four years before admission, when she began to have intermittent episodes of malaise, nausea and vomiting, chills, slight jaundice and frontal headaches, which lasted about two weeks and recurred at intervals varying from two weeks to six months. The earliest attacks were apparently precipitated by the eating of fatty foods, which had thenceforth been carefully avoided. During the attacks, the urine was dark, and the stools were frequently light colored. There was remission of jaundice between the episodes, with return to normal-appearing dejecta. The first few spells were accompanied by dull pains in the hips and back, but there were no such pains subsequently. In the few months preceding admission, the bouts of illness became severer and more frequent, and marked weakness began to appear. In the course of the four years, there was a loss of about 70 pounds in weight.

At no time in the illness was there hematemesis, melena or obvious fever. The patient denied any medication other than proprietary preparations of "bile salts" and "liver pills," prescribed by her physician.

The last episode started on an afternoon eleven days before entry, with abrupt onset of nausea and vomiting, followed by increasing malaise, weakness, jaundice and passage of dark urine. On the next day, the patient experienced shaking chills lasting for two or three hours; she did not feel feverish. In the following days, the chills recurred. Most of the stools were light colored, but some were green. There was progressive weakness, much severer than that on any previous occasion. Three or four days before entry, the abdomen became swollen and tender.

A brother of the patient had died of tuberculosis at the age of twenty-seven (when the patient was eighteen years old). The past history was otherwise of no interest. Until eight months before entry, the patient had worked in a factory, putting linings in shoes. She knew of no exposure to chemicals or fumes. She denied the use of alcohol.

On admission, the patient appeared emaciated, quite uncomplaining and free of discomfort. There was moderate icterus of the skin and scleras. The chest was emphysematous, with rales and slight dullness at the pulmonary bases. The size of the heart was within normal limits; the heart sounds were slightly distant. The abdomen was moderately distended and tympanitic, with shifting dullness and a demonstrable fluid wave. There were moderate external hemorrhoids. The skin showed diffuse, slight edema.

The temperature was 100°F., the pulse 110, and the respirations 24. The blood pressure was 118 systolic, 70 diastolic.

Examination of the blood showed a red-cell count of 4,150,000 with 13.7 gm. hemoglobin, and a white-cell count of 10,600 with 88 per cent polymorphonuclears. The blood Hinton reaction was negative. The van den Bergh reaction was biphasic, and showed 4.6 mg. bilirubin per 100 cc. The blood cholesterol was 172 mg. per 100 cc. The phosphatase was 25.7 Bodansky units, and the phosphorus 2.8 mg. per 100 cc. The serum albumin was 2.7 gm. and the serum globulin 4.0 gm. per 100 cc. The prothrombin time was normal. The hematocrit was 39.3 per cent. The bromsulfalein test showed 50 per cent dye retention.

The urine was normal except for the finding of bile by the foam test. The stools were pasty and soft green, with a positive guaiac reaction.

A roentgenogram of the chest showed elevation of the right diaphragm, with haziness in the right costophrenic angle. There were several areas of calcification in the right lower-lung field and hilus. Fluoroscopy demonstrated limited motion of the right diaphragm, in the correct direction, and absence of fluid in the right costophrenic angle. The diaphragm appeared pushed up by the liver. A roentgenogram of the abdomen showed enlargement of both the liver and spleen. There was no evidence of dilatation of bowel loops. The Graham test was positive.

On the sixth hospital day, a peritoneoscopy was performed.

DIFFERENTIAL DIAGNOSIS

DR. F. DENNETTE ADAMS: It seems unlikely that the chills reported were, in the strict sense of the word, real chills, for these do not last so long as two or three hours — nor do they often come more than twice daily. I should be inclined to interpret them as the chilly sensations that accompany rises of temperature.

Nothing is said about the size of the liver and spleen on palpation; enlargement of either or both could well have been overlooked because of unsatisfactory palpation due to abdominal distention. Before proceeding, we might learn from Dr. Lingley whether he believes that these organs were enlarged.

DR. JAMES R. LINGLEY: This is the film of the chest, showing the high right diaphragm with a shallow costophrenic angle. The lower hepatic border is not well visualized, but the liver is probably enlarged. The spleen, however, is not appreciably increased in size. The gall bladder is not visualized on any of the films, and the Graham test is therefore positive.

DR. ADAMS: I shall consider this problem first from the standpoint of jaundice. The causes of jaundice may be classified as hematogenous, obstructive and hepatogenous. Hematogenous jaundice, in this case, can be readily excluded. We are obviously not dealing with such disturbances as pernicious anemia, severe generalized sepsis and familial hematogenous jaundice. Stone in the common duct and cancer account for most cases of obstructive jaundice. If this patient had cancer of the head of the pancreas, lymph-node enlargement, which might occur in lymphoblastoma, or cancer of the biliary tract interfering with the flow of bile, the jaundice would have been progressive, not intermittent, and by this time would have been severer than the findings in this case indicate. Furthermore, the gall bladder would have been large and, even with the abdomen distended, might have been palpable. The duration of the illness was long for cancer. Stone in the common duct will be considered later.

Of the hepatogenous causes, one must consider some acute intrahepatic process such as catarrhal jaundice or toxic hepatitis, cirrhosis of the liver, diffuse neoplastic disease of the liver, such as lymphoma or carcinoma, and cholangitis with ascending infection into the liver. The duration was too long for any acute intrahepatic process, and diffuse neoplastic disease can be excluded by the same line of reasoning that I have applied to cancer involving the bile passages.

Of the various forms of cirrhosis, one need hardly consider that due to syphilis or cardiac disease, or pigment cirrhosis (hemachromatosis). There is nothing to point toward any of these.

Portal and biliary cirrhosis require further thought. The history is not suggestive of portal cirrhosis. There is no record of a previous acute liver ailment, nor is there any mention of alcoholism. The only suggestive points in favor of portal cirrhosis are the ascites and the laboratory evidence of impaired liver function. Bouts of pain simulating gall-bladder colic are not infrequently encountered in portal cirrhosis, but on the other hand, jaundice is not usually a feature except in the terminal stages.

The history of recurrent episodes of pain, jaundice, fever and gastrointestinal disturbance is perfectly typical of biliary cirrhosis. It is also typical of common-duct stone with intermittent obstruction. But biliary cirrhosis rarely occurs except in the presence of long-standing biliary-tract disease.

The laboratory tests — especially the high blood phosphatase, the low serum protein and the diminished excretion of bromsulfalein — indicate an appreciable degree of liver impairment, more than one would expect with common-duct stone alone unless the jaundice were of greater degree. By x-ray examination, the liver appeared large; the spleen may have been slightly enlarged — added evidence in favor of liver disease.

Since it seems impossible to explain all the changes on the basis of common-duct stone, one is forced to the conclusion that cirrhosis existed; if so, it must have been of the biliary type. But the presence of biliary cirrhosis presupposes previously existing obstruction or infection, and these would most probably be the result of stone in the common duct. The most likely diagnosis, then, in my opinion, is chronic cholecystitis with stones, stone in the common duct, ascending biliary-tract infection secondary to obstruction, and biliary cirrhosis secondary to the ascending infection.

One other problem deserves brief consideration. Could there have been carcinoma of the liver in addition? Primary carcinoma of the liver is not uncommon in cirrhosis and is rarely seen without cirrhosis. It is not commonly diagnosed ante mortem. One can suspect its presence in cases of cirrhosis when a definite mass can be felt in the liver, when a localized bulge of the diaphragm is discovered roentgenologically, or when metastatic cancer is discovered elsewhere. There was no evidence of metastasis, and the only hint of cancer in this case might be obtained from the roentgenologist. Dr. Lingley, should you consider the elevation of the diaphragm general, or do you think there is a localized bulge?

DR. LINGLEY: I should consider it either an enlarged liver or an infectious process beneath the dome of the diaphragm producing elevation and limitation; no definite localized bulge is apparent.

DR. ADAMS: Then I shall not add a diagnosis of primary carcinoma of the liver.

DR. TRACY B. MALLORY: Does anyone want to ask any questions or give suggestions at this point?

A Physician: It seems to me that we should give serious consideration to the possibility that this was carcinoma of the ampulla of Vater. That might explain the absence of pain and the itching, and waxing and waning frequently goes with it.

Dr. Mallory: The presence of a large amount of ascites with biliary cirrhosis would bother me a little bit.

Dr. Adams: It bothered me. Ascites is, of course, not common in biliary cirrhosis except in the terminal stages. Barring portal cirrhosis, which I do not believe existed in this case, I should say that the ascites is much more suggestive of carcinoma, but the evidence in favor of common-duct stone and biliary cirrhosis outweighs the doubt introduced by the ascites. Except for the ascites, the picture is typical of common-duct stone.

Dr. Wyman Richardson: If you will believe me, the patient did have ascites. I am sure of it.

Dr. Adams: It is too late for me to go on the other side.

Dr. Mallory: Dr. Richardson, do you want to comment before or after we have heard the peritoneoscopic findings?

Dr. Richardson: I should like to read the note that I made before peritoneoscopy was done. I think that is the fairest way. "Because of the history, I believe that this patient has had recurring biliary infection, perhaps with stone and with secondary biliary cirrhosis. She may have had recurring cholangitis and recurring focal liver degeneration, followed by distortion and ascites (end stage of toxic hepatitis)." I am attempting to explain the ascites, but rather poorly. "In spite of weight loss, in addition to high phosphatase, I doubt malignant tumor. If present, it must be secondary to primary liver disease, such as cirrhosis; and I cannot make out that the patient has a primary cirrhosis. Advise peritoneoscopy."

Dr. Mallory: Dr. Benedict, will you tell your gross findings?

Dr. Edward B. Benedict: I shall read my report: "Under local anesthesia, a 1-cm. incision was made in the midline just above the umbilicus, the peritoneal cavity inflated with air, and the Ruddock peritoneoscope introduced. Ten pints of slightly cloudy, straw-colored fluid was aspirated and sent to the laboratory. There were many adhesions between the edge of the liver and the abdominal wall. The liver did not appear enlarged. Multiple cystic implants were visible throughout the peritoneum — on the round ligament, on the wall of the bowel, on the brim of the pelvis and throughout the pelvis. There was also a cystic appearance to the surface of the liver, as if that also were involved in the process. The uterus was quite freely movable when examined by vagina and by rectum by Dr. McGahey. There were cystic implants on the surface of the uterus and on the broad ligaments. The ovaries could not be brought into view. There was considerable hemorrhagic appearance to the metastatic disease of the anterior abdominal wall overlying the lower abdomen and pelvis. Biopsy specimens were obtained from implants in the pelvis and from an area of the anterior peritoneum overlying the liver."

Dr. Mallory: What was your impression at the end?

Dr. Benedict: General carcinomatosis.

Dr. Mallory: Dr. Benedict's various biopsy specimens were examined histologically, and all of them showed tuberculosis.

Dr. Richardson: I shall read one further note, which I wrote after the peritoneoscopy: "I am not satisfied with the diagnosis of tuberculosis in this patient." I did not mean to say that I doubted the pathologist. I believed that the patient must have had tuberculosis, but that something else was present. I said: "If it is present, there must be another pathologic process. I believe that it is most probably tumor. There may also be cirrhosis of the liver." That is as far as I went.

Dr. Mallory: Do you want to make a further diagnosis, Dr. Adams?

Dr. Adams: I am very grateful for Dr. Richardson's support. I fail to see how tuberculous peritonitis can explain the whole picture. Nor can I make any diagnosis other than the one I have already made, on the basis of the evidence provided by the protocol. How could the jaundice be explained by tuberculous peritonitis?

Dr. Mallory: I am in a prejudiced position. I cannot explain it, however.

Dr. Richardson: And we could not on the service.

Dr. Mallory: One might imagine large tuberculous nodes pressing on the common duct, but I have not seen that in a case of tuberculous peritonitis, and I think it would be unlikely.

Clinical Diagnoses

Recurring biliary infection.

Choledocholithiasis, with secondary biliary cirrhosis?

Dr. Adams's Diagnoses

Chronic cholecystitis, with cholelithiasis.

Stone in the common duct.

Ascending biliary-tract infection (cholangitis), with infectious (biliary) cirrhosis of the liver.

Anatomical Diagnoses

Tuberculous peritonitis.
Miliary tuberculosis.
Pulmonary tuberculosis, healed.
Tuberculosis of hilar glands, healed.
Cholecystitis, chronic.
Cholelithiasis, choledocholithiasis.
Nephrosclerosis, moderate.
Operative scar, peritoneoscopy.

Pathological Discussion

Dr. Mallory: This patient continued to pursue a downhill course, and at autopsy we found, besides the tuberculous peritonitis, a gall bladder full of stones, and immensely dilated common bile and hepatic ducts. Twenty-eight stones were counted in the common duct. Gallstones unquestionably were the cause of the jaundice. There was a moderate degree of secondary cholangitis; it was on the border line of chronicity at which one begins to speak of biliary cirrhosis. There were also miliary tubercles in the liver and a great many in the spleen, which was consequently considerably enlarged, and there were scattered tubercles in the lungs. The primary cause of death was the generalized tuberculous infection.

CASE 28012

Presentation of Case

A twenty-nine-year-old housewife was admitted complaining of headache and diminished vision in both eyes.

She was perfectly well until three years before admission, when her first child was born. Although the delivery was normal, she vomited during the whole course of her pregnancy. At that time, she believed that her blood pressure was normal. After delivery, she had periodic attacks of vomiting, which six months later were accompanied by pains in both sides of the face, over the eyes and at the back of the neck. Vomiting began regularly a week before her period and lasted until the menses began. She was relieved during the time of flow, but vomited again for the following week. The pain lasted twelve hours, whereas the vomiting lasted a week. One year before entry, the patient again became pregnant. Her physician said that her blood pressure was high. During this pregnancy, she vomited constantly, had dizzy spells, and in the seventh month, began having throbbing pain over her entire head, with throbbing in the ears, especially after eating. She miscarried during the seventh month, but the emesis continued, and she lost weight steadily afterward. One month following the miscarriage, the blood pressure was 170 systolic, 120 diastolic, and the urine showed a heavy trace of albumin. During the next few months, headaches and vomiting continued, and the blood pressure ranged from 200 to 210 systolic, 130 to 140 diastolic. The patient returned to work, but gradually became weak and dyspneic. The menses ceased four months before entry. During these four months, she vomited at least once daily, the vomitus consisting of brown foul-smelling fluid but no blood. During the last three months, she occasionally blew clots of blood from her nose, but had no frank epistaxis; this partially relieved the headache. She also felt more drowsy during this period, objected to having people around her, and finally answered questions in a peculiar manner. One month before admission, she suddenly noticed decreased peripheral vision and could not read well, mainly because of blurring. Three weeks before entry, she was seen in the Out Patient Department. The blood pressure was 210 systolic, 118 diastolic. The urine showed a specific gravity of 1.004, 2 white blood cells and a few epithelial cells per high-power field, and a slight trace of albumin. The red-cell count was 2,900,000 with 50 per cent hemoglobin, and the white-cell count was 12,500. The patient was to return later for study. Two weeks later, constant slight epistaxis began. Three days before entry, muscular twitchings were noted. One day later, the ankles began to swell. She had lost 34 pounds in weight during the previous year.

The past and family histories were noncontributory.

Physical examination showed a well-developed but emaciated, dehydrated young woman, with a pasty, pale appearance, who lay quietly in bed. She was stuporous, answered questions with difficulty and at times did not respond at all. The pupils were normal. The fundi showed tortuous vessels with arteriovenous nicking. The disks were somewhat blurred. Exudate and a small hemorrhage were seen near the macula in the left eye. The tongue was dry and brown, and the mouth covered with sordes. The breath was strongly ammoniacal. Examination of the lungs was negative except for a few coarse rales at the bases. The left border of the heart was 10 cm. to the left of the midline. The apical rate was 140; there were occasional extrasystoles and a marked pulsus alternans, only the stronger beats reaching the wrist. A precordial friction rub was heard. The veins were full but collapsed at the level of the auricle. The liver edge was palpable 3 cm. below the costal margin, and the upper edge was at the sixth interspace. The deep reflexes were sluggish. Occasional muscular twitchings were noted in the extremities.

The temperature was 98°F., the pulse 120, and the respirations 10. The blood pressure was 160 systolic, 90 diastolic.

Examination of the urine showed a specific gravity ranging from 1.004 to 1.014, a large trace of albumin, and 0 red cells, 20 to 30 white cells and many squamous epithelial casts per high-power field. The blood showed a red-cell count of 2,600,000 with 50 per cent hemoglobin, and a white-cell count of 9200 with 91 per cent polymorphonuclears. The nonprotein nitrogen of the serum was 310 mg. per 100 cc., the chlorides 82 milliequiv. per liter, the carbon dioxide combining power 37.2 vol. per cent, and the protein 7.6 gm. per 100 cc. A lumbar puncture showed normal findings.

The patient rapidly failed and died one day after admission.

Differential Diagnosis

Dr. Asiton Graybiel: First of all, I shall briefly discuss and attempt to evaluate certain features of this history that are either of interest in themselves or contribute to the making of a diagnosis.

It would be of help to establish the duration of the illness. The first symptoms, nausea and vomiting, occurred three years before death, during the entire course of the patient's first pregnancy. I am not sure why she vomited — perhaps because of toxemia or neurosis. I believe it is unusual for a patient to have vomiting due to toxemia throughout pregnancy and yet deliver a normal baby — abortion or miscarriage is the rule.

We do not know how long the patient had hypertension before death. She thought that her blood pressure had been normal during her first pregnancy, but she was probably asked the question directly and was not quite sure of the answer. The first definite knowledge of hypertension was near the beginning of the second pregnancy, one year before death. The patient was twenty-eight years of age at that time, which is very young for one to have developed essential hypertension with its sequelas. This immediately arouses the suspicion that the primary disease was in the kidneys. If kidney disease is related entirely or almost entirely to pregnancy, it tends to disappear, and the patient becomes well, once the uterus is emptied. In this case, vomiting continued, and the high blood pressure persisted following miscarriage.

The history states that "during the last three months, she occasionally blew clots of blood from her nose . . .; this partially relieved the headache." It seems impossible that the loss of such small amounts of blood would be important in this respect.

During the last three months of life, the patient became drowsy and mentally deranged; in the light of later developments, this was obviously due to uremic poisoning. Later, she developed twitchings, whose immediate cause was thought to be disturbances in calcium metabolism.

The urinary findings observed three weeks before death are especially interesting in that there was only a slight trace of albumin and 2 white blood cells and no red blood cells per high-power field.

I might point out that the swelling of the ankles noticed three days before death need not necessarily be explained on the basis of heart failure. This swelling may have been due to capillary damage as a result of the high degree of toxemia. The rales heard over the lung bases might be explained on the same basis.

The changes in the retinas and retinal vessels deserve especial note. A small amount of exudate was observed in one eye, the vessels were tortuous, and only one small hemorrhage was seen. In the malignant phase of essential hypertension, the retinal changes are much more marked, and this fact is a strong argument against this diagnosis.

The history states that "there were occasional extrasystoles and a marked pulsus alternans, only the stronger beats reaching the wrist." I have never observed this phenomenon, but in turning to the literature I found that Lewis* says that it can occur. Nevertheless, I doubt the accuracy of the observation in this case. An electrocardiogram might have shown that the weaker beats were regularly occurring extrasystoles. Without this record, there is some chance for confusion, especially when it is remembered that, in pulsus alternans, the interval between the small and large pulses is shorter than that between the large and small.

A precordial friction rub is not uncommonly heard in uremia. It is due to fibrinous pericarditis and is a grave prognostic sign.

The nonprotein nitrogen was 310 mg. per 100 cc., which is an extremely high value. This is final proof of the existence of marked kidney failure. Whenever the nonprotein nitrogen attains the level of 200 mg. or more, it may be safely concluded that the functional capacity of the kidneys is about nil. The low value for chlorides represents chloride depletion as a result of vomiting. The carbon dioxide combining power of 37.2 vol. per cent is proof of acidosis.

If this case is considered in a straightforward fashion, the facts suggest that the patient had developed glomerulonephritis some time in the

*Lewis, T. *The Mechanism and Graphic Registration of the Heart Beat.* Third edition. 529 pp. London: Shaw and Sons, Ltd., 1925. P. 434.

past, and that, at the time of pregnancy, symptoms and signs of kidney failure appeared. During the second pregnancy, she became very toxic. The blood pressure was markedly elevated, probably as a result of the kidney insufficiency. She developed uremia despite the fact that the uterus was emptied, and I think she died with uremic poisoning. There is nothing that would lead one to suspect that the patient had had essential hypertension in the past and died in the malignant stage of the disease. Apparently the heart was somewhat enlarged, but there is no clearcut evidence of congestive failure; the edema over the shins and the rales in the lungs could be satisfactorily explained on the basis of uremic poisoning. The coronary vessels were probably in quite good condition. The microscopic appearance of the myocardium may prove to be abnormal simply because of toxemic changes. A curious type of myocarditis associated with uremic poisoning has been described.

DR. PAUL D. WHITE: I quite agree that there probably was not a true pulsus alternans in this case but that a bigeminal rhythm due to extrasystoles accounted for the failure of alternate pulse waves to reach the wrist. I have examined a good many cases of pulsus alternans and have not found any in which the pulse has actually failed to reach the wrist. However, it does appear that there was marked cardiac enlargement, which is a background for true alternation of the pulse.

Should one expect to find anything wrong with the cerebral blood vessels? It is possible that the patient had edema of the brain or, as so often happens, small hemorrhages. I do not know whether the brain was examined, but I should think that either of these possibilities might be mentioned.

DR. FRANCIS R. DIEUAIDE: I should like to raise the question whether, in spite of the age of this patient, renal damage on a vascular basis should not be considered. It is true she was young, but certain findings suggest the possibility. One is the nature of the urinary findings. If one takes them seriously, the low specific gravity, with the small amount of albumin and relatively insignificant sediment content, seems to me to point toward that type of chronic renal condition rather than chronic nephritis on a previous glomerular basis.

DR. GRAYBIEL: I remain unconvinced that the patient had essential hypertension, which had developed into the malignant stage. Under such conditions, she might well have shown even more abnormality in the urine than she did. If she had nephrosclerosis of fairly short duration, she might well have had many red cells and a great deal of albumin in the urine. Sometimes, in chronic glomerulonephritis, the urinary findings are not very remarkable. I think that the inconspicuous eyeground findings are also somewhat against the diagnosis of a severe grade of malignant hypertension. I still favor the diagnosis of a chronic glomerulonephritis, aggravated particularly by the pregnancy.

CLINICAL DIAGNOSES

Glomerulonephritis.
Uremia.
Hypertensive heart disease, with congestive failure.

DR. GRAYBIEL'S DIAGNOSES

Chronic glomerulonephritis.
Uremia.
Arterial hypertension.
Cardiac hypertrophy, slight to marked.
Uremic pericarditis.

ANATOMICAL DIAGNOSES

Chronic glomerulonephritis.
Cardiac hypertrophy, left ventricular.
Pericarditis, acute fibrinous, uremic.
(Uremia.)

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Very often, at postmortem, when the kidneys on gross examination are so shrunken that it may be impossible to make a definite diagnosis, even the pathologist has great difficulty in making a decision. In the ordinary type of malignant vascular nephritis in a woman of twenty-nine, the kidneys would not decrease in size to the degree of a chronic glomerulonephritis. The kidneys in a patient with malignant vascular nephritis rarely shrink to less than two thirds the normal weight, in contrast to chronic glomerulonephritis, in which the kidney weight may be less than one fourth the normal.

This patient had chronic glomerulonephritis. The kidneys weighed 90 gm., and microscopically there were innumerable hyalinized glomeruli, with crescent formation, which is characteristic of chronic glomerulonephritis. There was a uremic pericarditis of the so-called "bread-and-butter" type, thick fibrin strands producing interadherence between the two layers of pericardium, and 50 cc. of straw-colored fluid. The heart was hypertrophied and weighed 400 gm. The hypertrophy was for the most part left ventricular and was undoubtedly secondary to the nephritis. There was nothing of significance in the other organs, and no sign of heart failure.

226
32

ENROLLMENT FORM FOR PROCUREMENT AND
ASSIGNMENT SERVICE FOR PHYSICIANS

Dr. Sam F. Seeley, Executive Officer
Procurement and Assignment Service
New Social Security Building
4th and C Streets, S.W.
Washington, D. C.

Dear Dr. Seeley:

Please enroll my name as a physician ready to give service in the Army or Navy of the United States when needed in the current emergency. I will apply to the Corps Area commander in my area when notified by your office of the desirability of such application.

Signed_____

1. Give your name in full, including your full middle name:
2. The date of your birth:
3. The place of your birth:
4. Are you married or single?
5. Have you any children? If so, how many?
6. Do you believe yourself to be physically fit and able to meet the physical standards for the Army and Navy Medical Corps?
7. Have you filled out previously the questionnaire sent to all physicians by the American Medical Association?
8. When and where were you graduated in medicine?
9. In what state are you licensed to practice?
10. Do you now hold any position which might be considered essential to the maintenance of the civilian medical needs of your community? If so, state these appointments:

11. Have you previously applied for entry into the Army or Navy Medical Service? If so, state when, where and with what result (if rejected, state why).

Signature_____

Date_____ Address_____

The New England
Journal of Medicine

Formerly

The Boston Medical and Surgical Journal

Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

Editorial Board

Joseph Garland, M.D.
William B. Breed, M.D.
George R. Minot, M.D.
Frank H. Lahey, M.D.
Shields Warren, M.D.
George L. Tobey, Jr., M.D.
C. Guy Lane, M.D.
William A. Rogers, M.D.
Stephen Rushmore, M.D.
Henry R. Viets, M.D.
Robert M. Green, M.D.
Charles C. Lund, M.D.
John F. Fulton, M.D.
A. Warren Stearns, M.D.
Dwight O'Hara, M.D.
Chester S. Keefer, M.D.

Associate Editors

Thomas H. Lanman, M.D.
Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year, Boston funds; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Friday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

A CALL TO SERVICE

War has already greatly increased the need of the United States Army and Navy for medical officers, and as pointed out in an editorial in the December 18 issue of the *Journal*, appreciable numbers of medically trained men are required for service in other governmental agencies. Because of this, a meeting of the Procurement and Assignment Service, in conjunction with the medical-preparedness committees of the American Medical Association, American Dental Association and American Veterinary Medical Association, was held in Chicago on December 18, to devise means for making available to the Army and Navy the names of all physicians, dentists and veterinarians who are willing to enroll immediately in governmental service. Although this information was requested on the questionnaires sent out by the American Medical Association, the forms had no official status and were filled out at a time when the United States was not an active participant in the war. Furthermore, the amendment of the Selective Service Act to include all men under forty-five years of age places many more physicians in the group of those who may be called for active service.

For the convenience of physicians who are willing to serve the Nation in the event of need, an enrollment form that was carried in the December 27 issue of the *Journal of the American Medical Association* is reproduced on the opposite page. On receipt of the forms by the Procurement and Assignment Service, each enrollee will be classified according to information already available in the national roster of physicians at the headquarters of the American Medical Association, and so far as possible, assignment will be made to the type of service for which he is best suited. It is obvious that adequate medical service to civilian communities, public-health agencies and industrial plants must be continued, and committees are already being established in corps areas, states and counties to ensure the proper distribution of physicians.

To wage war successfully, all groups must be prepared to make great sacrifices, and it is to be expected that the medical profession — trained in a code of selfless devotion to duty — will accept this call to service with the cheerful readiness that it has shown in the past.

BLOOD-PROCUREMENT SERVICE

At the request of the Surgeons-General of the United States Army and Navy, the American Red Cross and the Division of Medical Sciences of the National Research Council have co-operatively organized a blood-procurement service for the purpose of supplying the medical departments of the Army and Navy with human blood plasma. Thus far, six procurement centers are in operation in eastern United States, and five others are in the process of organization. During the past year, sufficient blood has been obtained in Boston to fill

the needs of a pilot plant for the production of crystalline human albumin under the direction of Prof. E. J. Cohn, of the Department of Physical Chemistry, Harvard Medical School.

Now that war has been declared, the activities of the Boston Procurement Center must be tremendously increased to supply blood for conversion to dried plasma, and the prewar quota of 17,000 donors within the next five or six months is but a fraction of what will eventually be needed. Quarters have been established at 691 Boylston Street, a personnel has been trained, and 100 donors are being bled daily. The organization of the procurement center and the technics used are those adopted as standard for the country by the American Red Cross and the National Research Council, and the final product meets all the requirements of the National Institute of Health.

Great care is exercised in selecting the donors. They must be twenty-one to sixty years of age and in good health. They are acceptable only if they have a hemoglobin level of 80 per cent or higher and a systolic blood pressure lying between 100 and 200 and if they have not been bled within eight weeks. Mature minors may be accepted as donors with the written permission of a parent or legal guardian. Five hundred cubic centimeters of blood is taken from donors of average size, and the facts that the repeat donor percentage is high and that reports from employers indicate that mass bleedings at manufacturing plants have not decreased the workers' efficiency indicate that this amount has caused no ill effects.

This meritorious project deserves the wholehearted support of the medical profession, because it not only provides an essential means of saving human life but also affords every citizen an opportunity to make a worth-while contribution to the war effort. A ready response will augment the growing morale of the armed forces and do much to crystallize *esprit de corps* among civilians.

MEDICAL EPONYM

Ludwig's Angina

Wilhelm Friedrich von Ludwig (1790–1865) communicated his vivid description of "a variety of inflammation of the neck which has recently been of frequent occurrence in this community" to the *Medicinisches Correspondenz-Blatt des württembergischen ärtzlichen Vereins* (**6:** 21, 1836). A portion of the translation follows:

> After a series of prod mal symptoms . . . there develops a firm swelling . . . usually in the cellular tissue surrounding the submaxillary gland. This . . . swelling spreads around the neck under the jaw . . . with marked lateral bulging. . . . The tongue lies on a floor of . . . indurated bright-red tissue, which feels like a hard, calloused ring along the inner border of the jaw inside the mouth. . . . Ability to open the mouth is restricted and painful . . . speech is difficult . . . thick and gurgling. . . . The skin, . . . in the early stages at least, is very slightly reddened if at all and is normal in texture; . . . later, soft red spots may appear . . . but no pus is ever formed. . . . The symptoms of the subsequent rapid course are those of a putrid-typhoid process, and in four to five days, the tenth to twelfth from the onset of the illness, coma develops and death occurs with indications of respiratory paralysis.
>
> R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

At the annual meeting of the Council of the Massachusetts Medical Society, held in May, 1941, a resolution to establish a committee on maternal welfare was passed. This resolution also empowered the President to name a committee whose membership should represent geographically the various sections of the State. The resolution was presented to the Council by members of the Section of Obstetrics and Gynecology because it was believed that, to carry on some phases of the work that had come before the section, a committee having delegated authority should be established. In accordance with this vote, the President appointed the following committee: Dr. Judson A. Smith, chairman, Boston; Dr. Thomas Almy, Fall River; Dr. Robert L. DeNormandie, Boston; Dr. M. Luise Diez, Boston; Dr. Christopher J. Duncan, Brookline; Dr. M. Fletcher Eades, Boston; Dr. Arthur F. G. Edgelow, Springfield; Dr. Rachel L. Hardwick, Boston; Dr. Joseph W. O'Connor, Worcester; Dr. Louis E. Phaneuf, Boston; Dr. George M. Shipton, Pittsfield; Dr. Warren R. Sisson, Boston; Dr. Richard M. Smith, Boston; Dr. Raymond S. Titus, Boston; and Dr. Richard J. Williams, Lynn. This committee has met and organized. The chairman, Dr. Judson A. Smith, was appointed by the President; the secretary, Dr. Titus, was elected by the committee.

In October, 1941, a meeting of the Executive Committee of the Section of Obstetrics and Gyne-

cology was held in Boston. It was the opinion of this committee that, since a committee on maternal welfare had been appointed, much of the work that the section had carried on should be relinquished to this committee, an official body of the Massachusetts Medical Society. Hence, the study on maternal welfare, which the Section of Obstetrics and Gynecology has conducted for the past five years, was turned over to the Committee on Maternal Welfare, as of December 31, 1941, and from now on, all work of this type, except that pertaining to arrangements for the annual meeting of the section, will be handled by this committee. The case histories that have been appearing in the *Journal* will continue, at least for the time being. In next week's issue of the *Journal*, a résumé of the study of maternal deaths during 1940 will appear.

MEDICAL SOCIAL SERVICE FOR THE HANDICAPPED CHILD*

In these weekly broadcasts, sponsored by the medical profession, you have heard from a great many physicians and public-health authorities about the advances in medical knowledge. You have been given information, important to every intelligent person, concerning the common diseases and their care.

As one long associated with the medical profession in service to patients, I want to share with you some of my experiences as a medical social worker in a large medical institution where specialization in the many branches of medicine is to be found. Medical social service is established in most of our big hospitals and clinics. You may well ask what social service has to do with medical institutions. Any of you who have had experience with sickness yourselves or have had illness in the family know how disturbing sickness can be. Often, it is more than pain and distress. It upsets our regular way of life. It may mean that we must stop work, lose time at school or give up some special pleasure we had anticipated. These experiences are common to us all.

Fortunately not all of us have had the more serious diseases, which are well known in our great hospitals and to the medical profession, sicknesses that mean that the patient may not be able to work again or that he must learn to live with a chronic disease that may have to have treatment over a long time. I have in mind a girl with diabetes, who must learn to control her diet habits and who may have to take insulin every day for many years. I think of the boy with infantile paralysis, who must have many months and possibly years of muscle training — possibly operations. He may have to learn to walk with braces. And I think of the child who has lost his precious eyesight.

Does all this bring sad pictures to your minds? If it does, I wish you could know as I do many of the courageous, cheerful men, women and children who have been able to face such sicknesses, who have done their part in getting well or, if not well, in still finding that life can be very much worth while.

As one such courageous patient said, "It's not what is gone, but what is left for me that counts now." Sometimes, sickness and the way the patient takes it are the means of opportunities for a fuller life. It is a curious fact that it may take such experience to awaken us to what we may be. I am thinking of a fine, active young boy, a leader in sports, who was stricken with infantile paralysis at fourteen years of age just as he was about to enter high school. For a time, the future seemed very black to him. But, under skillful medical care and through his own determination to do his exercises regularly, he was able after two years to get about with crutches and braces. But this improvement in the condition of his body was only part of this boy's problem. What about his eager, active mind? What about his education? What can he ever do to support himself? He is not the kind of person who wants to be dependent on others. Herein the medical social worker could help the patient and the doctor. For the doctor, too, wants the patient to be restored to useful living. Accordingly, arrangements were made for his education first in a specialized school for handicapped children, where the floors are not slippery for crutches and braces, and ramps are used instead of stairs. He has made a good record through seven years and with the help of a generous person he is now in college preparing for journalism.

The other day, a boy came from a distant town to one of the clinics for examination of his ear. His mother reported that he had been considered dull in school and had to repeat his grade. His parents considered him a bright enough child but thought he did not pay attention when he was spoken to. Finally, one of his teachers suggested that he was not hearing well and advised the parents to have him examined. At the clinic, his hearing was carefully tested, and it was found that he heard nothing with the right ear and that the left was defective. For this boy, several things can be done. A letter to the teacher advises that he sit in the front row on the right side of the room, so that his left ear can be used as much as possible. Then lip reading instruction can be started, so that he may learn to depend on his good eyes more than his defective ears for understanding what people say. Periodic examination of his left ear will be made. Let us hope that he has no further loss of hearing. But it will be well to have some aptitude tests to see in what line he has special ability. He should be guided into the kind of work he is fitted for by nature so that his handicap may be minimized.

Perhaps many of you have your own family doctor. If you do, you know how much more he does for you than make a diagnosis and order medicine. He is an adviser and friend who helps you face the problems that sickness brings. But in our great clinics where patients go who have no family doctors, or our great hospitals to which many people are sent for care, it has been found necessary to have a person who can spare the busy doctor's time and give patients counsel in their difficulties and practical help in working out their problems.

Massachusetts, like many other states, is much concerned about helping people who are in trouble — whether it is support for those who are destitute, protection for neglected children, education of the handicapped, blind or deaf, medical care for crippled children, or for the patients with tuberculosis, cancer and those with mental diseases, rehabilitation of those who can be trained for special work, protection of workers from the hazards in industry, compensation for those injured at work. Then, too, through generous citizens there are many privately

*A "Green Lights to Health" broadcast given through Station WAAB by Miss Ida M. Cannon on Saturday, November 22, and sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

supported resources to supplement the public agencies, resources for help in difficult family problems, foster homes for children who cannot be in their own homes, hospitals, clinics, centers for recreation and agencies for helping those who come from across the seas to seek new homes in our land. The medical social worker must be very familiar with all these resources. Her knowledge and skill in helping people to help themselves is called on every day as physicians in our great medical institutions ask her assistance for patients under their care. But if she is a well-trained social worker, she wants every citizen to be self-reliant. She wishes each home to be a center for strength in the family ties, not only when all goes well but also in times of trouble. When she is facing a problem with a patient, it is her purpose to help the patient to help himself, to help the family to meet the problem. Her experience with many similar problems, her knowledge of resources for help when the difficulties cannot be met by the patient and the family alone may be needed. Did you ever notice that when people are not well and things look black, they are inclined to think in circles? They come back to the same place again; it is not real thinking. Worry is a more suitable word for it. Such people need help in straight thinking. They need to have a plan for meeting their problems, whatever they are. It is in this planning how to meet the difficulties that arise with sickness that medical social service may be useful.

Let us take for example the child who is found to have rheumatic heart disease. There are many hundreds of such patients in New England. When the disease is active, the doctor usually tells the patient and his mother that he must stay quietly in bed for weeks, sometimes for months. There may be little or no physical pain for the patient to bear, but he must accept restriction of his activities and loss of school and play that may be more difficult to bear. Medical social service is called on by the doctor to help the mother and patient not only in carrying out the medical orders but also in making a plan with them for a way of life that may have special compensations. To meet the many needs of this family, several services are available. A visiting nurse can teach the mother how to give the child in bed the necessary care, how to keep track of his temperature, how to prepare his food. Massachusetts provides for visiting home teachers to continue education of children who are not able to go to school yet are able to do some homework. If the teacher is not available, there are often people who are willing to act as volunteer tutors for such children. But there is also the question of recreation. Children must be taught to play quiet games, to make things with their hands. Often, the child discovers abilities in modeling, painting or belt weaving that he never knew before. Or in these weeks in bed, he may be led to discover the great privileges we have in our public libraries. Reading may become a new resource for him, not only for information, but for romance and adventure. Through books, he may find that he can travel to far lands and learn of the lives of great men and women of history.

To be really healthy, we must be healthy both in body and mind. We should be making full use of all the capacities God has given us. How few of us do that! Sickness may sometimes be made a real teacher. We discover, for one thing, how precious good health is. But, if we must live with physical limitations, we have freedom to develop our minds, and through use of our latent capacities, we may find compensations for misfortune. This is what many children have taught me. I am grateful to them for their teaching.

WAR ACTIVITIES

UNITED STATES ARMY

The following medical officers entered on active duty between November 29 and December 13, 1941:

Wiesner, Ernest E., 1st Lieut., of Brockton, Massachusetts: Camp Edwards, Massachusetts.

Raymond, William H., Jr., 1st Lieut., of Lynn, Massachusetts: Fort Williams, Portland, Maine.

CIVILIAN DEFENSE

Dr. Augustus Thorndike, owing to the call into active service of General Hospital No. 5, has been obliged to resign from the position of deputy medical director of the Medical Division of the Massachusetts Committee on Public Safety, and Dr. A. William Reggio, of Brookline, has been appointed to the post.

MISCELLANY

AIMS OF COLLAPSE THERAPY

The habit of calm appraisal characteristic of English physicians seems to be ruffled neither by the pressure of war emergencies nor by howling bombs. Tuberculosis work in England, although sometimes interrupted, continues to engage the earnest attention of physicians and laymen. American readers will profit by Pearson's clear analysis of the objects of collapse therapy in the treatment of pulmonary tuberculosis (Pearson, S. V. What are we aiming at in collapse therapy? *Tubercle* 22:159–165, 1941), an abstract of which follows:

The objects of treatment in pulmonary tuberculosis are fourfold: to arrest the progress of the disease, to heal the damaged tissues, to restore the general health and working capacity of the patient, and to render his sputum negative. Often, there is likelihood of clash between these objects, and what to do is sometimes overshadowed by the question when to do it. The aims of collapse treatment for pulmonary tuberculosis may be surveyed under eight heads.

The constitutional effects of this disease are of more importance than the local. The constitutional symptoms, rather than damage to the lungs, endanger life and health. But the successful treatment of the local lesion is the way to allay the constitutional symptoms. The characteristic feature of the disease, a series of reactions in the connective tissues, only secondarily affects the functions of the breathing apparatus. It is the exudative lesions that produce the most dangerous symptoms, and are most amenable to collapse therapy, although it is not yet known how such therapy affects them.

Its chief characteristic is that it produces reactions in the connective tissues. Aside from its effect on gross lesions, including cavities, collapse therapy produces ischemia, passive hyperemia and lymphatic stasis, which encourage proliferation of connective tissues and the production of fibrosis in early lesions. It is well to emphasize this because collapse therapy is too often reserved for the patient with excavation and other gross lesions. The relaxation, the ischemia and the lymphatic stasis affect the diseased parts more than the healthy. But, if the toxemia is lessened, the work of healthy lung tissues is eased because

the function of the latter is interfered with less than it was.

The tubercle bacillus is nearly always "master of ceremonies." It is a mistake to be apprehensive of secondary organisms within the lesions in the lung, for the tubercle bacillus is the all-important etiologic agent. It is time the bogey of mixed infection was laid to rest. The tubercle bacillus is responsible not only for early infiltration of the Assman type (early round foci) or early excavation, but also for liquefaction.

A re-expanded, healed lung should be the aim of therapy when and as far as possible. This means that a reversible and temporary type of collapse is to be preferred whenever possible.

The best induced collapse is always a selective one. So-called "respiratory traumatism" (abnormal stretching of diseased parts) is based on the idea that the movements of respiration do harm to a diseased lung and that collapse treatment counteracts this harm by resting the lung. But on occasion collapse treatment may increase the harm, for example, when a stretched pleural adhesion attached viscerally to the region of a cavity in the lung occurs in an artificial pneumothorax. It must ever be an aim of collapse therapy to amend and convert such a condition. The mechanisms that produce harm are those which increase the stretching of diseased parts. These must be discovered with the aid of roentgenograms and, even more, by careful observations, on the screen, of respiratory movements. (Slow-motion cinematography is being increasingly employed in the study of respiratory movements.)

Collapse is obtained by relaxing tension of diseased parts. This has long been emphasized, but even now, when movements during breathing and coughing are being studied, too much attention is often given to cavities rather than to the influence of such movements on the relaxation of other pulmonary tissues.

The movements of respiration affect the diseased parts of the lung either directly or indirectly — a distinction not always easy to make. The surrounding parts can be pulmonary or nonpulmonary, and their effect on the tensions within the thorax must be considered. Collapse therapy aims at relieving these and permitting relaxation. Perhaps even more important than expansion, contraction and movement of cavities is the effect of respiratory movements on the lung tissues surrounding and in proximity to a cavity.

In dealing with cavities, one's aim is, of course, to get rid of them. Collapse plays a part in this by closing the bronchocavernous passage; stabilizing and reducing intracavitary pressures; starving and debilitating the tubercle bacilli on the cavity walls.

"It always strikes me," says the author, "that the hole in the lung has held far too much of the attention." Efforts to classify cavities have been useful but not inconclusive. One is often in doubt how to interpret an annular shadow. Mistakes are still made between a ring of fibrosis, a zone of reaction around a central focus and one of atelectasis. Even the supposed hole may be found to be no hole on post-mortem examination. There are other difficulties. Probably the best classification of cavities is that of Coryllos: open, closed and narrowed.

Early cavities disappear sometimes without any measure to relax anything. When a cavity does not close spontaneously, collapse therapy is used. Artificial pneumothorax would succeed more frequently if the suitable case were found earlier and proceeded with, especially if cauterization of adhesions were more popular. The excavated lung needs relaxation from without, that is, by being detached from the bony cage of the thorax; but air under too high a pressure within the cavity itself can keep the hole open, and if such air is absorbed and the compressed lung around the cavity re-expands it will fill the gap. This process is accomplished by getting the bronchial opening blocked and may occur more or less by accident. Cavity closure after an ineffectual pneumothorax occurs fairly frequently, and can be aided by a temporary phrenic operation, but the reason why the cavity closes cannot be explained. Closure may come about through a kinking of the bronchus draining the cavity although a case has been reported in which a kinking had a disastrous effect. One's aim should be to know when a kinking has occurred, when it is benefiting the patient and how it has come about.

Several lessons can be learned for collapse therapy from work with Monaldi's method, namely, the transpleural decompression treatment of cavities. One of these has to do with the blocking of the cavity. When a cavity becomes blocked, the oxygen is absorbed, and the tubercle bacilli languish. There is good evidence to show that an aim of treatment should be to starve and debilitate the tubercle bacilli on the walls of the cavities. When that has been achieved, it remains for means to be found to allow the pericavernous tissues, either by expansion or indirectly by their contractile powers, to close the cavity.

The prevention of the discharge of the bacilli. Cavities are the main, if not the only source of the expectorated positive sputum, which augments the danger of bronchogenic spread and spread to other persons. An essential aim of treatment, therefore, is to prevent the discharge of tubercle bacilli. But the restoration of health must come first; a well-trained ex-patient who behaves sensibly is not a danger. The restoration of the patient to work must not be forgotten in the desire to eliminate cavities and positive sputum.

Finally, aims should always be based on clinical and x-ray observations, which should not be directed too exclusively to cavities or to the lung condition. Collapse therapy is not purely mechanical. The many factors of the situation must be taken into account. Knowledge of collapse treatment is advancing quickly and modifying medical practice. That is the ever-fascinating interest of medicine. As it progresses, certain problems are solved and discussion about them ceases, but new ones arise. — Reprinted, with changes, from *Tuberculosis Abstracts*, December, 1941.

BOOK REVIEWS

The Political Life of the American Medical Association. By Oliver Garceau. 8°, cloth, 182 pp., with 14 charts. Cambridge: Harvard University Press, 1941. $2.50.

This curious book is a good example of faulty, armchair reasoning. Apparently, the author has read widely the official publications of the American Medical Association, including the *Proceedings*, and also many publications of the various state medical journals, to which he gives repeated reference. He has also corresponded, according to his acknowledgment in a preface, with the secretaries of state and county societies, and with Olin West, secretary of the American Medical Association. Apparently, he has never taken the trouble to attend the annual sessions, particularly those of the House of Delegates, nor has he investigated at first hand the numerous activities of the association in its Chicago headquarters. His book, therefore, is decidedly lacking in factual background, and is practically valueless as an authentic or even important contribution to the subject. It would pass unnoticed ex-

cept for the fact that it emanates from the Department of Government, Harvard University, and was published by the Harvard University Press. This, indeed, appears to give it some authority. With this setting, one is surprised to find many statements of doubtful authenticity: paragraphs in which the actual meaning of a situation is twisted to make the author's point, a journalistic style not well fitted to what purports to be a scientific, logical discussion of the subject, and such a biased point of view that it takes away any force that the author might have in argument. This jejune product cannot be recommended as a book worthy of serious study.

Infantile Paralysis: A symposium delivered at Vanderbilt University, April, 1941. Lecture 1. *Poliomyelitis.* 8°, cloth, 239 pp., with 46 illustrations and 2 charts. New York: The National Foundation for Infantile Paralysis, Incorporated, 1941. $1.25.

In April, 1941, a series of six lectures on poliomyelitis was given at Vanderbilt University under the auspices of the National Foundation for Infantile Paralysis. These lectures have now been published, and since they were given by the leading authorities in this country on various aspects of the disease, the volume presents a report on the current opinions regarding etiology, diagnosis and treatment. The essays are remarkably uniform in both style and scholarship. Because nothing of a similar nature is available in medicine and because of the timeliness as well as the broadness of these contributions, this book is an important contribution to the subject. Great credit should be given to the National Foundation for Infantile Paralysis in arranging these lectures and seeing that they were issued in printed form. The book is excellently printed, with adequate bibliographies and an index. It sells for a fraction of its actual cost.

Electrocardiography in Practice. By Ashton Graybiel, M.D., and Paul D. White, M.D. 8°, cloth, 319 pp., with 272 illustrations. Philadelphia and London: W. B. Saunders Company, 1941. $6.00.

It is becoming increasingly apparent that the electrocardiograph is one of the great achievements of the twentieth century. It makes the heart sign on the dotted line and describe some of its ailments. Yet it is not an instrument on which one may press a button and have the diagnosis appear; nor is it merely a tool of the cardiologist. Rather, like the ophthalmoscope and the microscope, the electrocardiograph is an indispensable instrument in the hands of the clinician. As a result of the research that has been done, an extensive literature has accumulated on the subject. The practicing physician whose interest in cardiology has been aroused and who wishes to make the electrocardiograph part of his armamentarium finds himself in a daze. The periodic literature on electrocardiography is vast and scattered, and it is impossible for the novice to get a clear conception of the subject. Nor does the average book on cardiology cover the subject of electrocardiography sufficiently. On the other hand, some of the best books on electrocardiography are cumbersome, because of the amount of space given to the technical principles involved.

This book seems to be an answer to many a physician's prayer. It is a practical book on electrocardiography, unfettered by needless theory. The authors have eliminated the detailed descriptions of the various types of electrocardiograms, the details of technic and the underlying physiologic principles involved. After a brief introduction, the book deals with the interpretation of electrocardiograms, normal as well as abnormal. As the authors have rightly stated, "Errors in electrocardiographic interpretation are probably more often made by calling normal variations abnormalities, than by missing real abnormalities when they are present." The authors give records of all types of variations from the normal. Practically every heart disorder is represented, including such factors as drugs that affect the electrocardiogram, or such miscellaneous conditions as anemia and trauma. Each record is printed on the right side of the book, and a short history of the patient, with an interpretation of the picture, is given on the opposite side. This is as it should be: the electrocardiogram is part of the entire clinical picture. The second part of the book is devoted to electrocardiograms for interpretation. These are records without labels, on which the physician can test himself. It is an excellent source of self-instruction. One can check himself by reading the interpretation and the history on the opposite page. Among textbooks on electrocardiography, the book stands out as one of the most practical and comprehensive. It is a valuable addition to any clinician's library.

The Doctor Takes a Holiday: An autobiographical fragment. By Mary McKibben-Harper, M.D. 8°, cloth, 349 pp., with 17 illustrations. Cedar Rapids, Iowa: The Torch Press, 1941. $2.50.

Dr. McKibbin-Harper, well known for her previous travel books and for her close association with the work of the American Medical Women's Association, describes in this book her many travels to Europe and to the Orient. Her chief interest was naturally in medical conventions in which women played a prominent part, and in visits to women physicians in various parts of the world. In this book, one finds much material of value, and it is indeed a record of extensive travels by one who had an appreciative mind and who could evaluate conditions, particularly in the Orient. The illustrations are of considerable importance, since they show pictures of medical scenes, hospitals and doctors rarely found in other medical books. The volume is rather poorly printed, and there are numerous minor errors that should have been corrected. In general, it is a fairly interesting travel book by a physician.

Clinical Aspects of the Electrocardiogram, Including the Cardiac Arrhythmias. By Harold E. B. Pardee, M.D. Fourth edition, revised. 8°, cloth, with 219 illustrations and 14 tables. New York: Paul B. Hoeber, Incorporated, 1941. $5.75.

The fourth edition of this popular text maintains the high standard set by its predecessors. In the eight years that have elapsed since the previous edition, new developments in the field of electrocardiography have taken place at such a rapid pace that it has been necessary practically to rewrite the whole book. In particular during this period, various thoracic leads have established their usefulness in practice, and perhaps the most important new feature is the consideration given to the precordial leads in persons with normal and with diseased hearts. The bibliography that accompanies each chapter has been selected with discrimination, and furnishes in itself a valuable guide to anyone wishing to go deeper into the subject. The book is thoroughly practical in its orientation and is presented in such a way as to be useful even to the beginner in the field.

(Notices on page x)